FIGURE 1

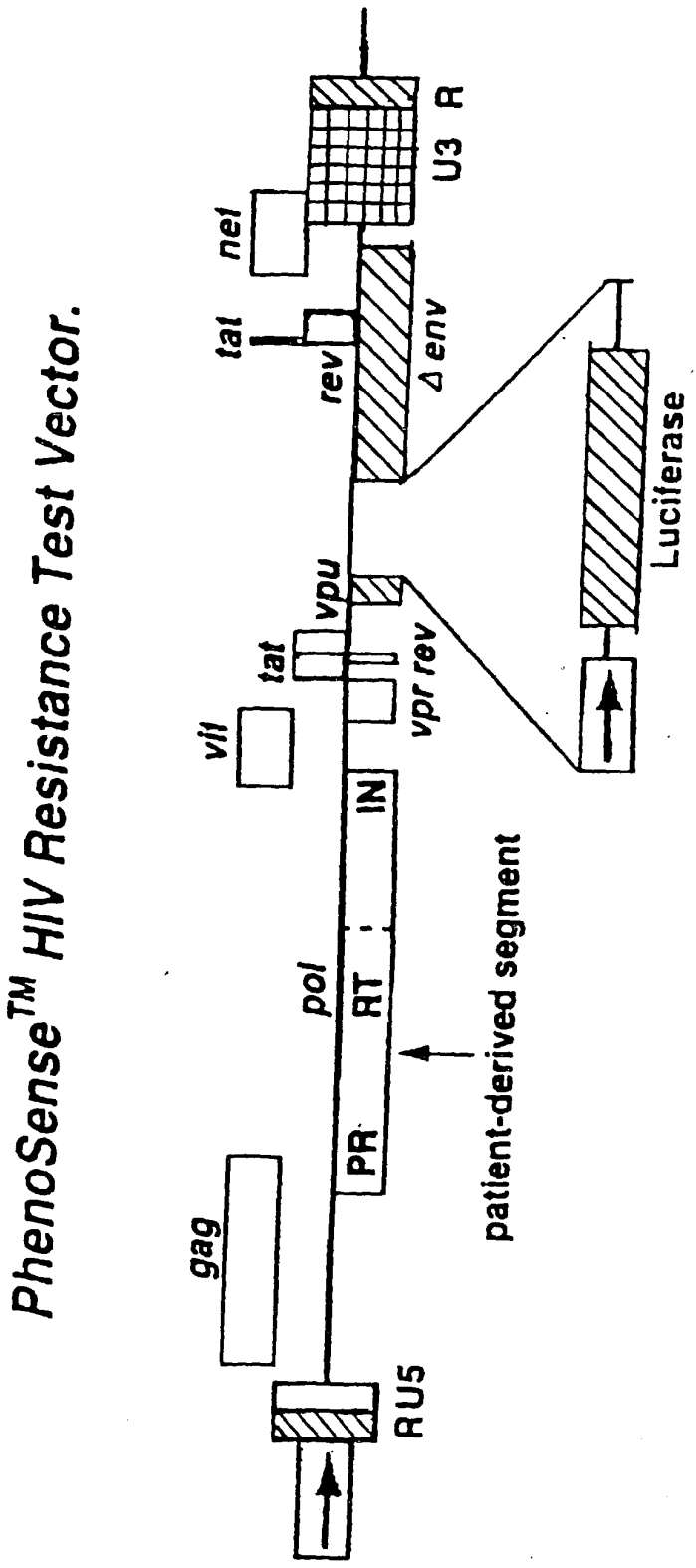
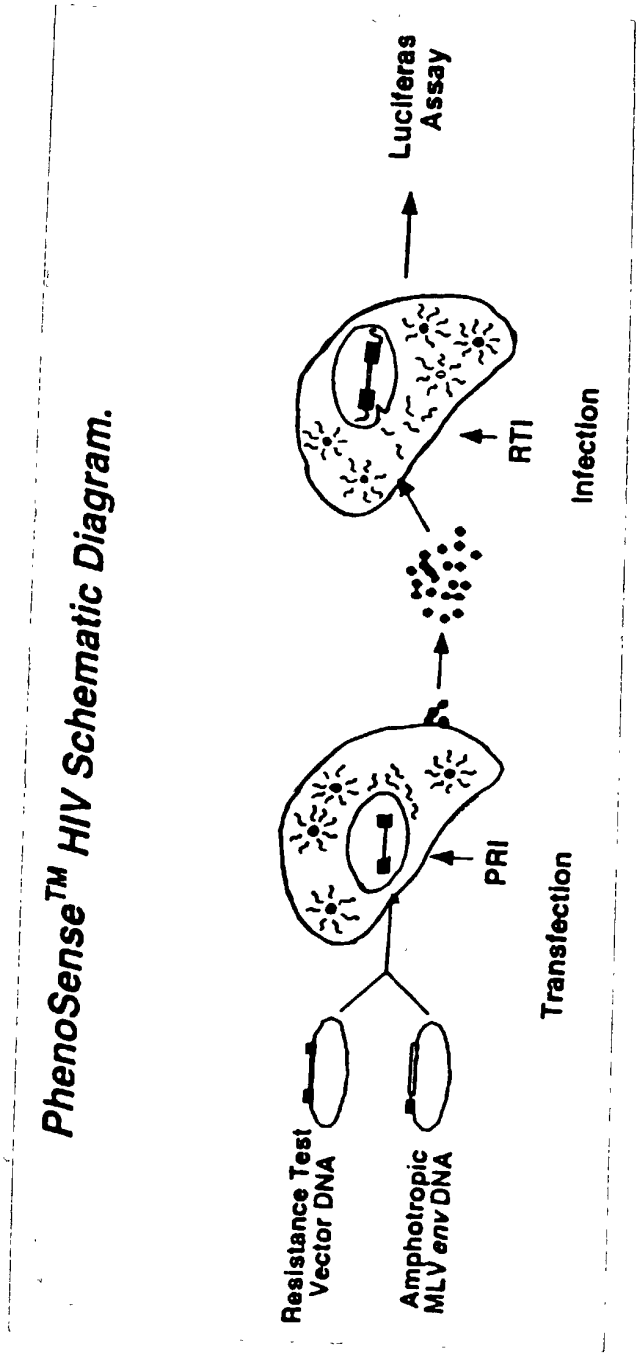
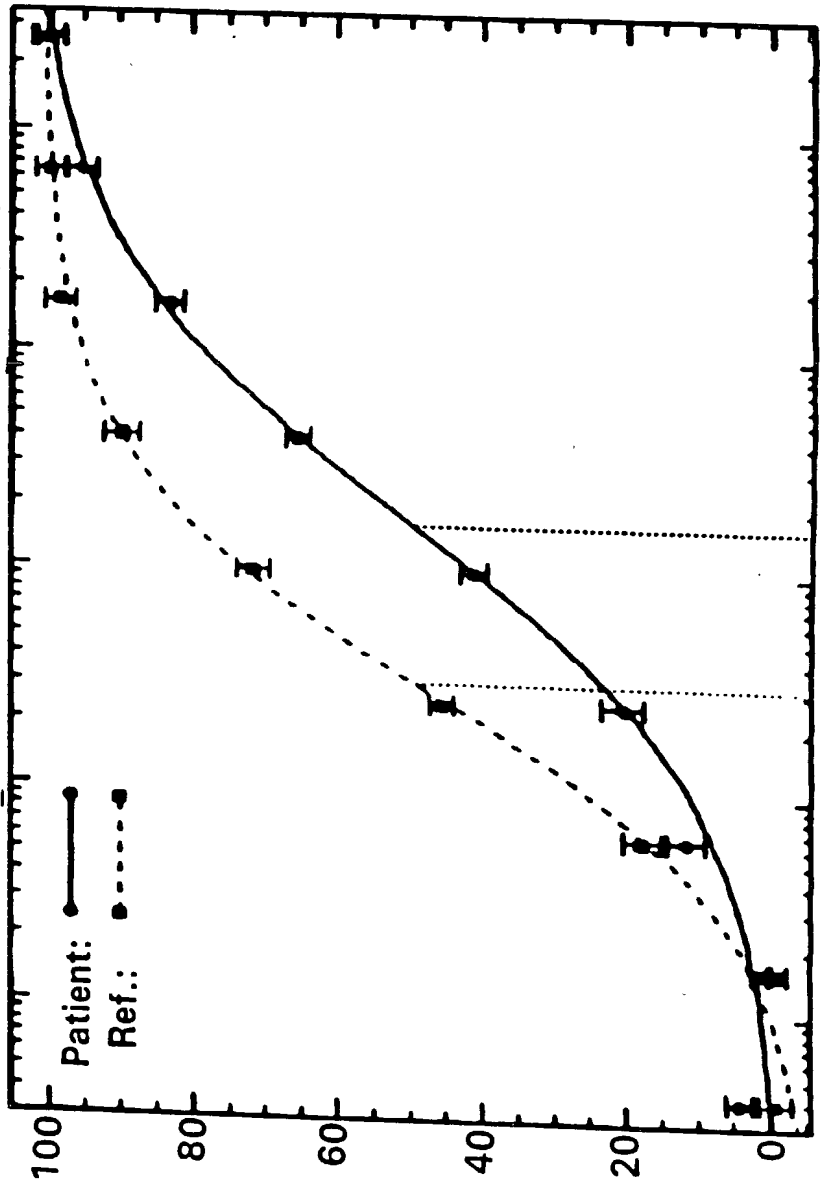


FIGURE 2

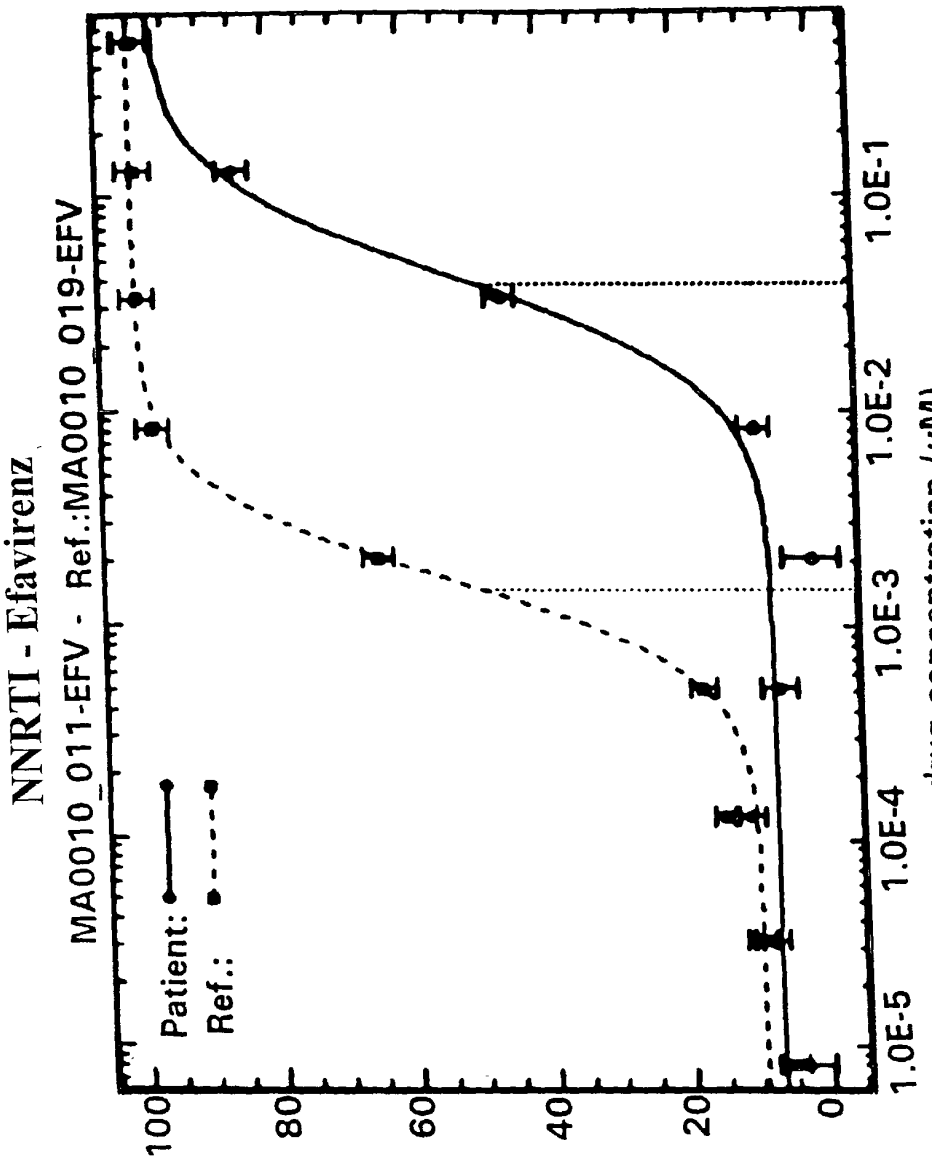


3/50



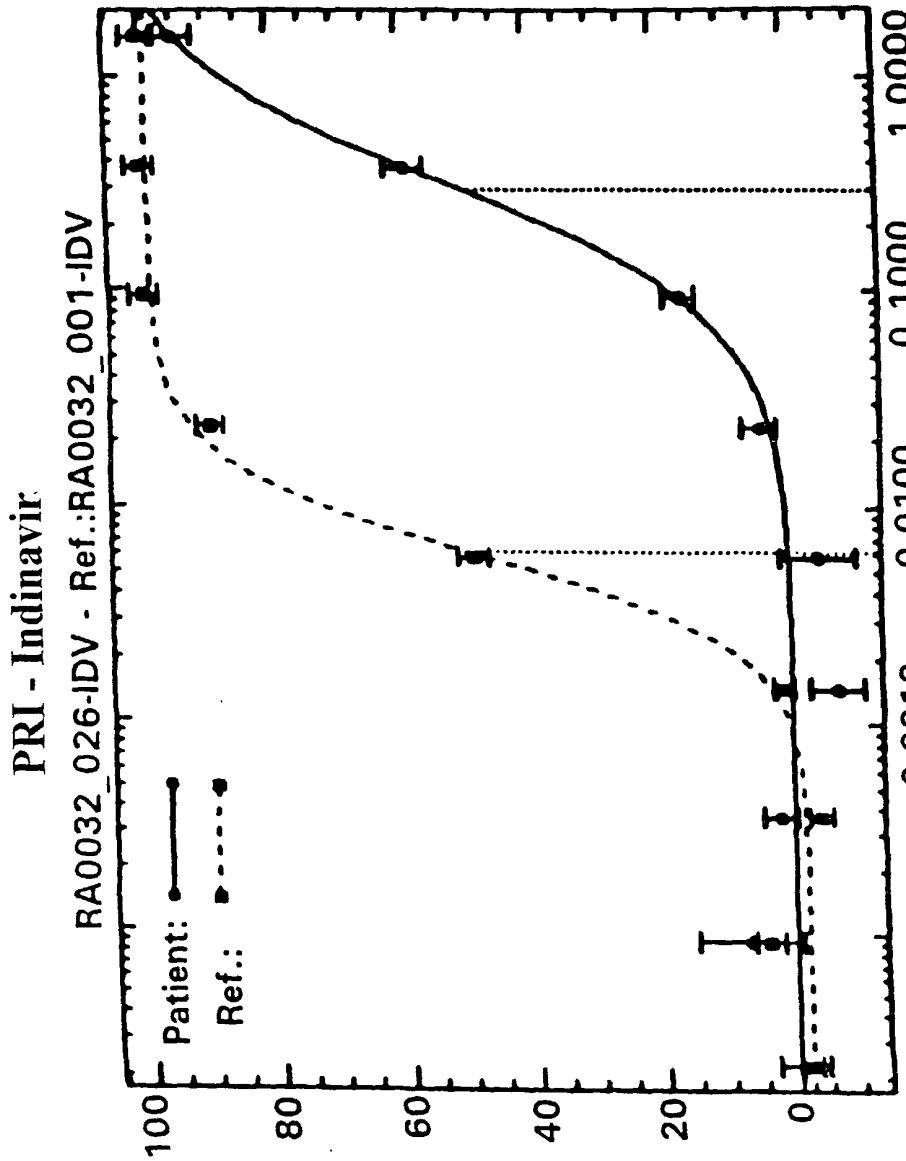
AZT-Control IC_{50} = *0.032*
AZT-Patient IC_{50} = *0.170(5.2-fold)*

FIGURE 3A



EFV-Control IC_{50} = *0.0015*
EFV-Patient IC_{50} = *0.0380(25.6-fold)*

FIGURE 3B



IDV-Control IC_{50} = *0.0062*
IDV-Patient IC_{50} = *0.2935(47.4-fold)*

FIGURE 3C

FIGURE 4A

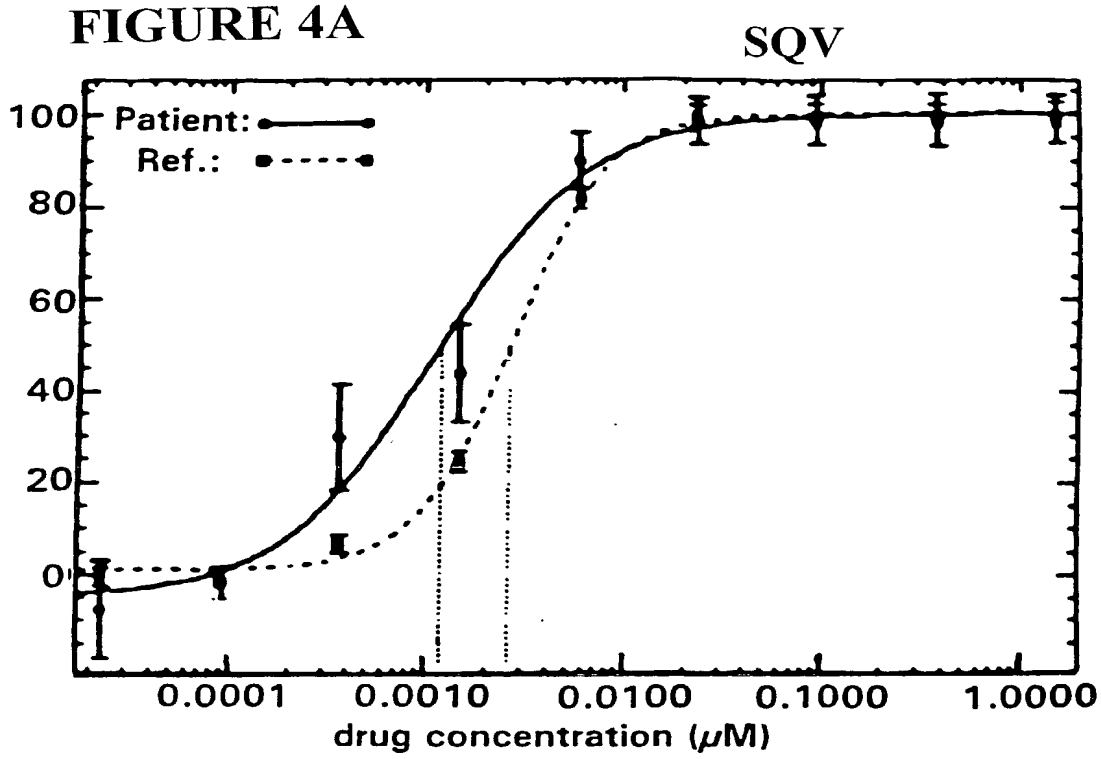


FIGURE 4B

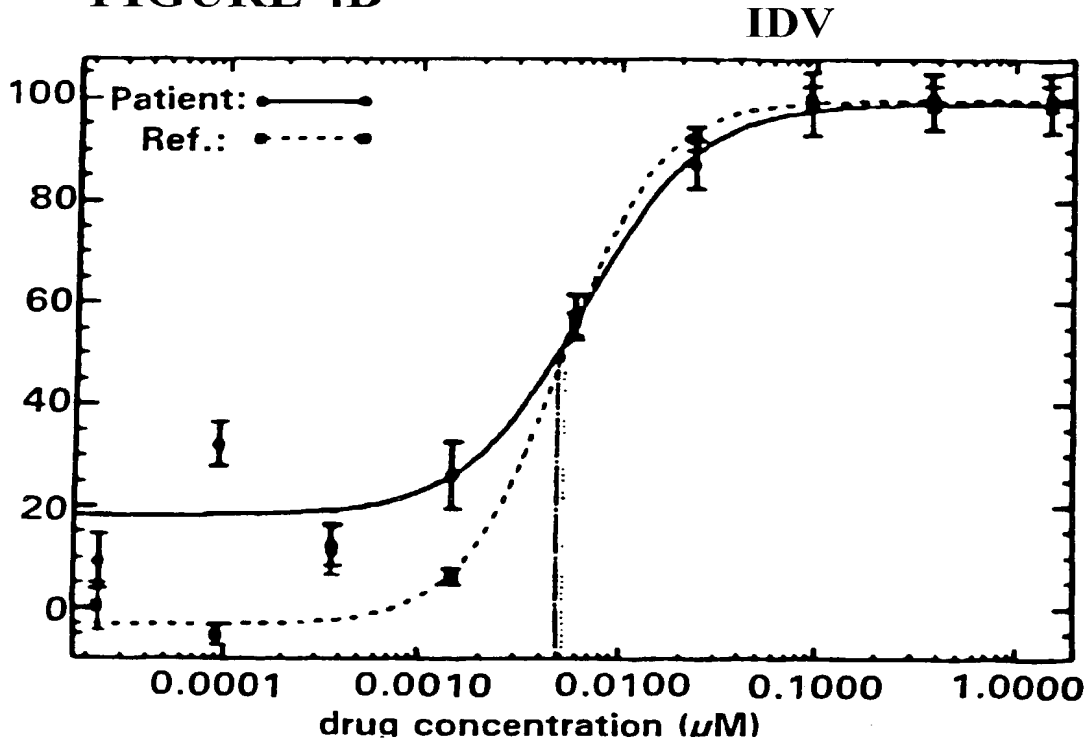


FIGURE 4C

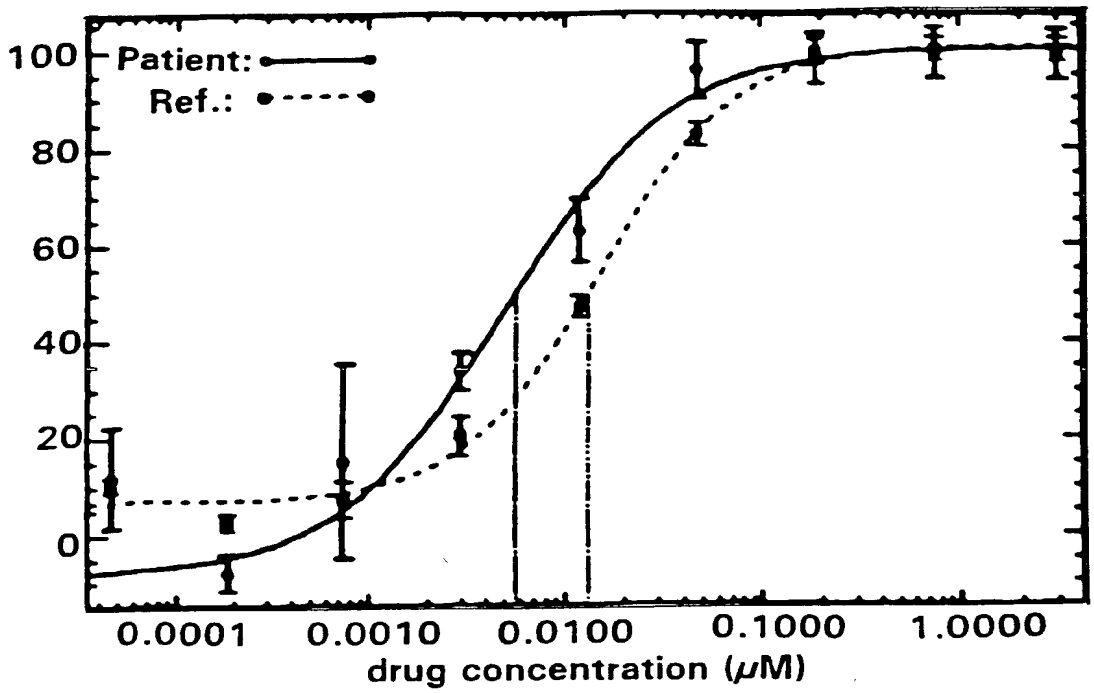
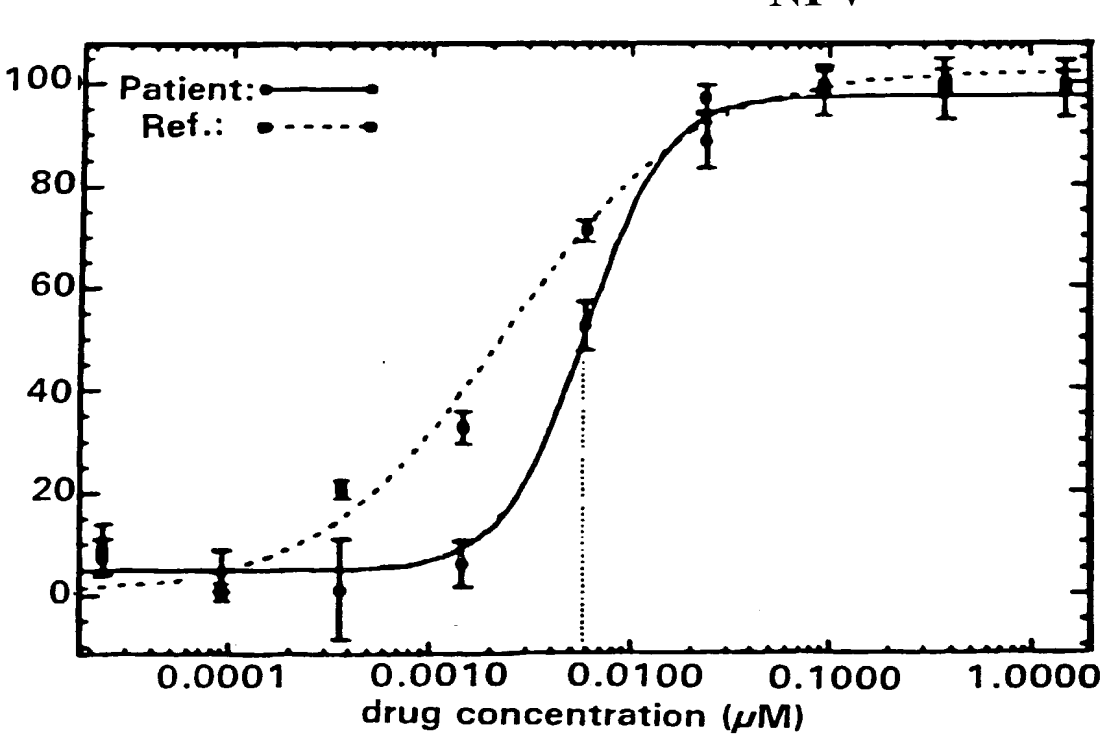


FIGURE 4D



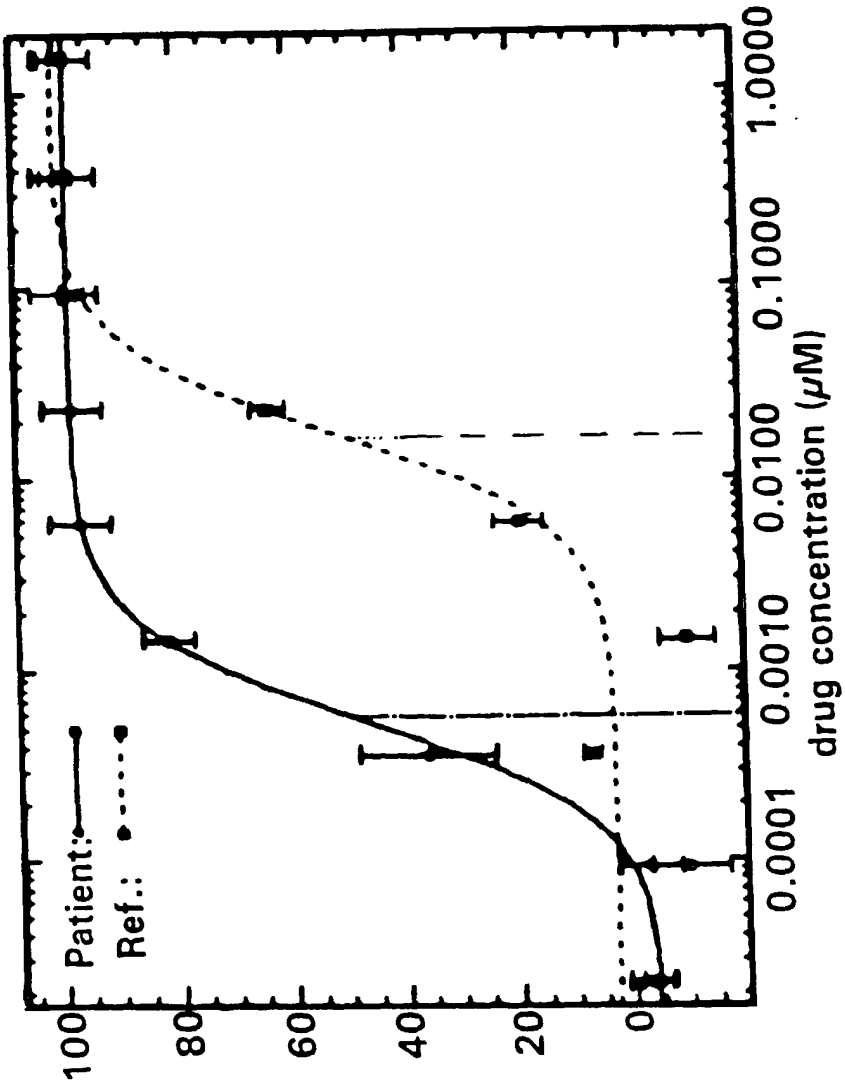


FIGURE 4E

FIGURE 5A

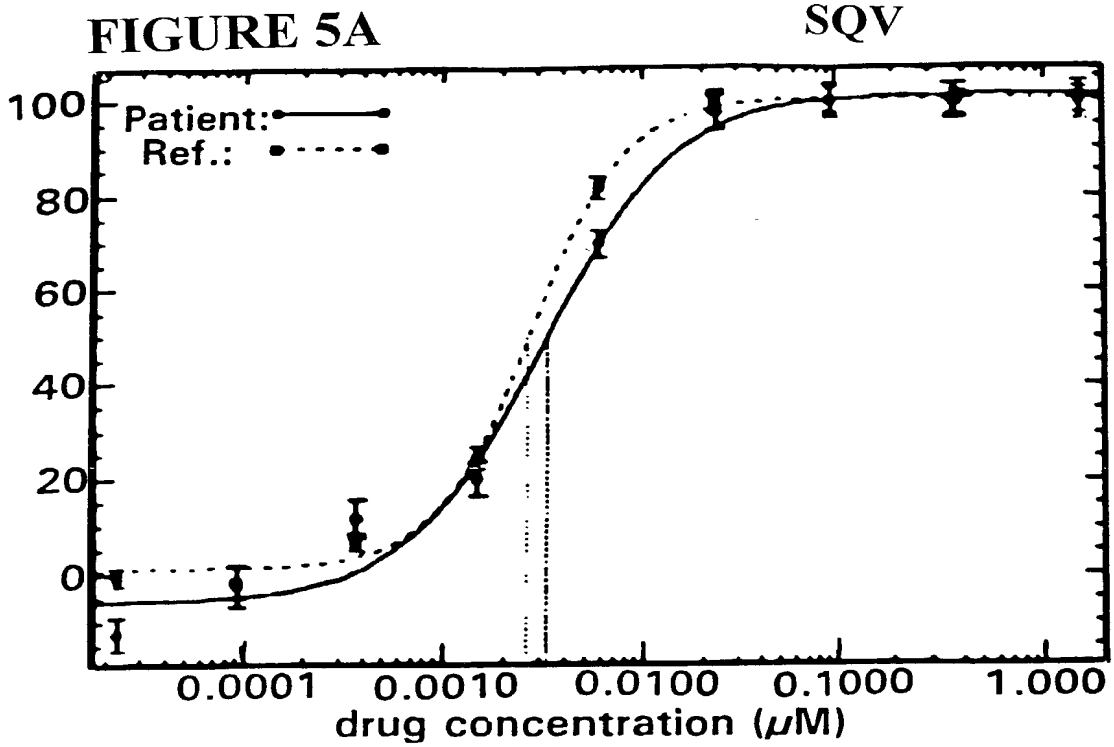


FIGURE 5B

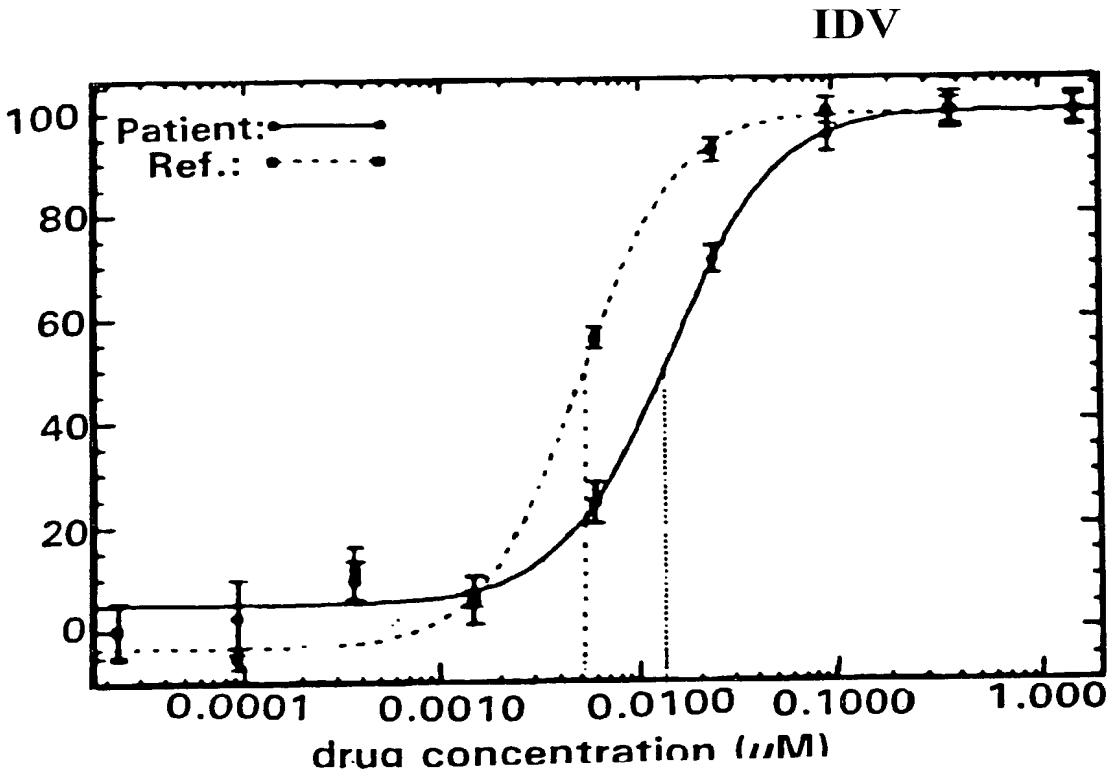


FIGURE 5C

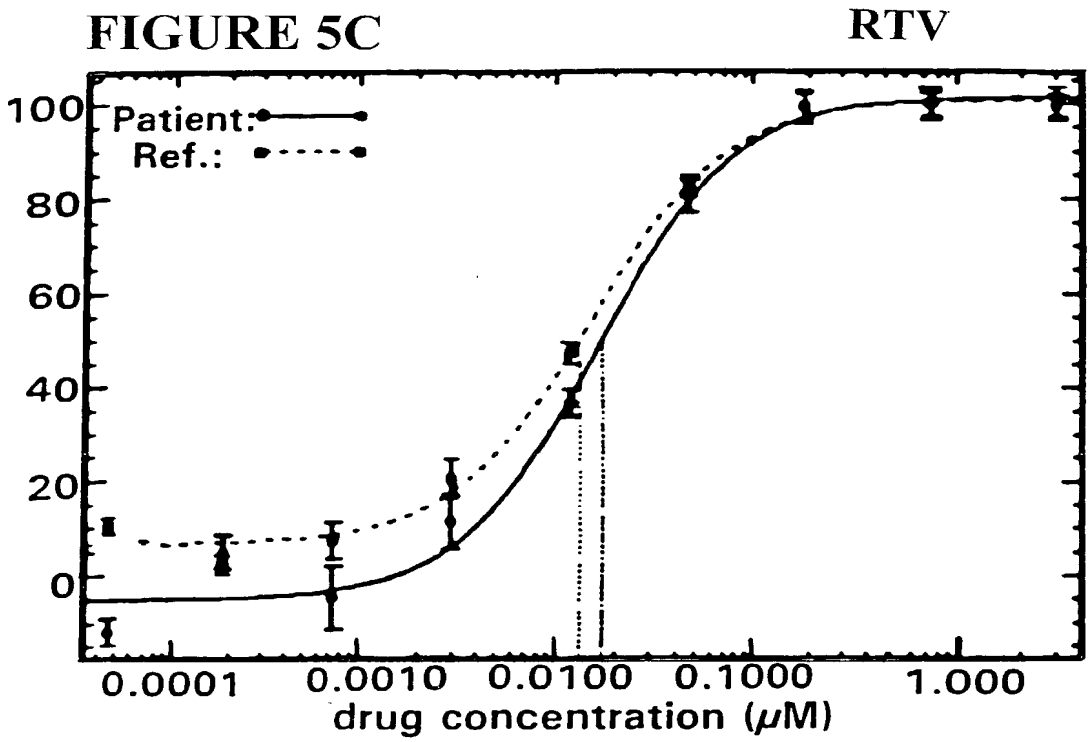
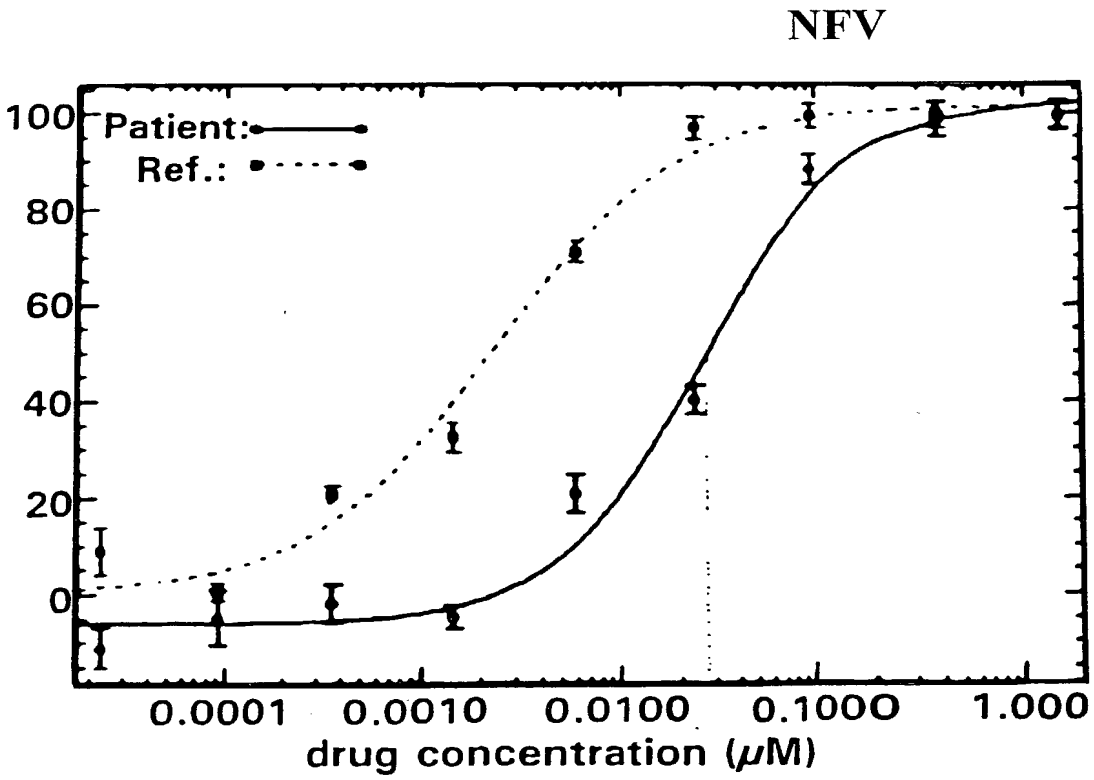


FIGURE 5D



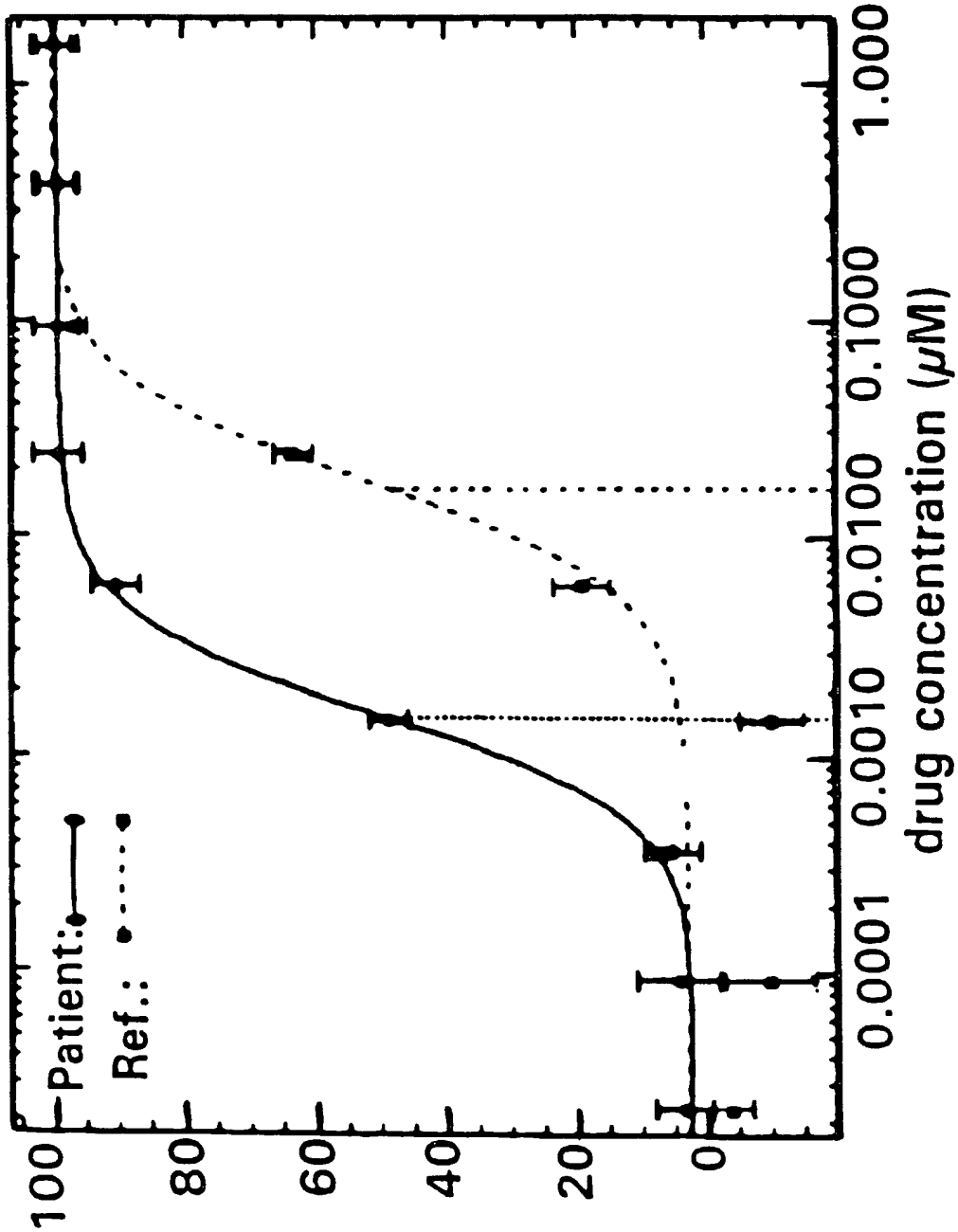


FIGURE 5E

FIGURE 6A

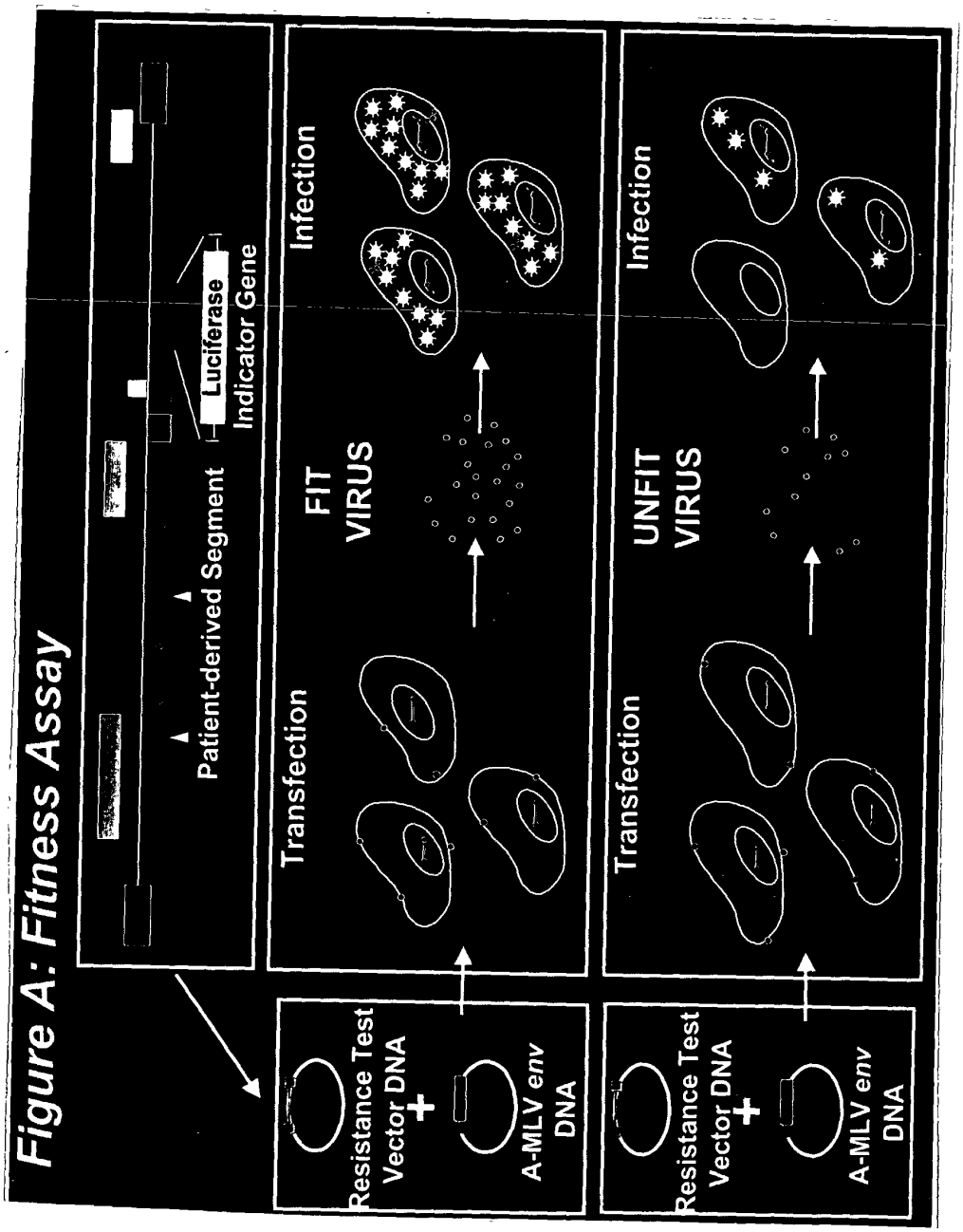


FIGURE 6B

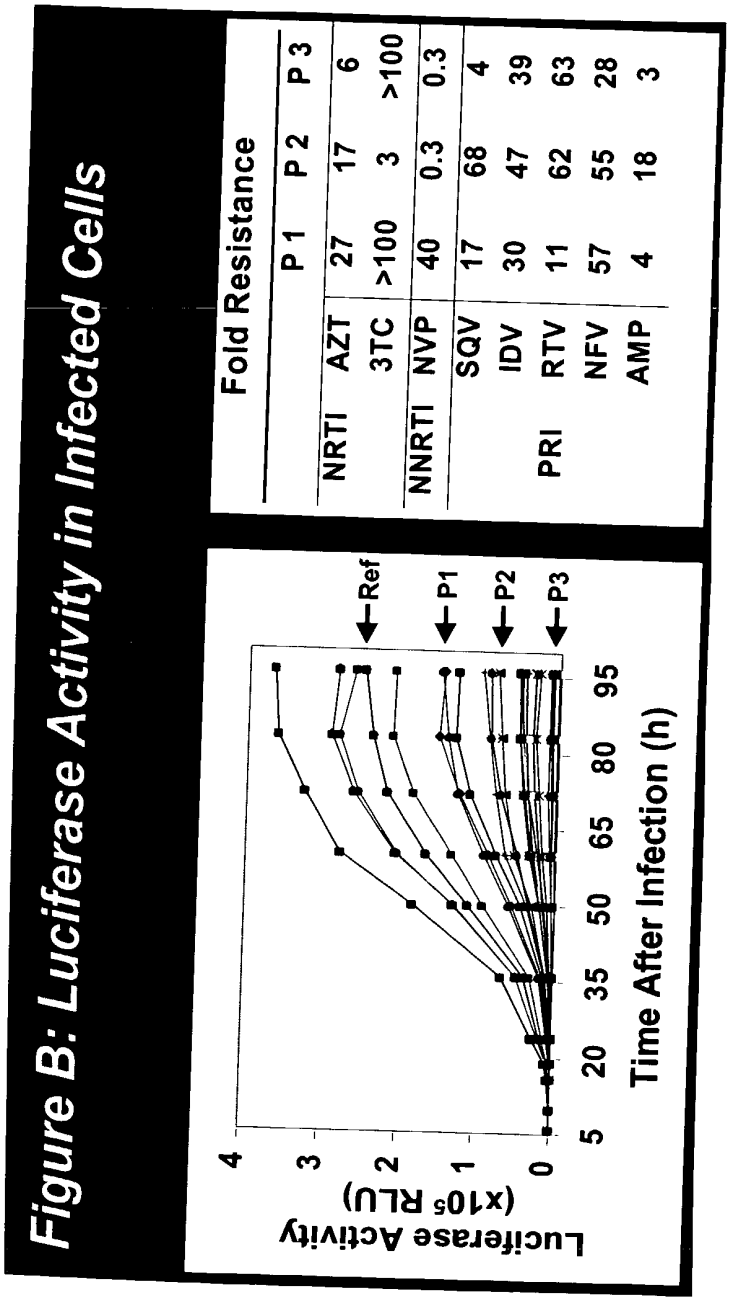
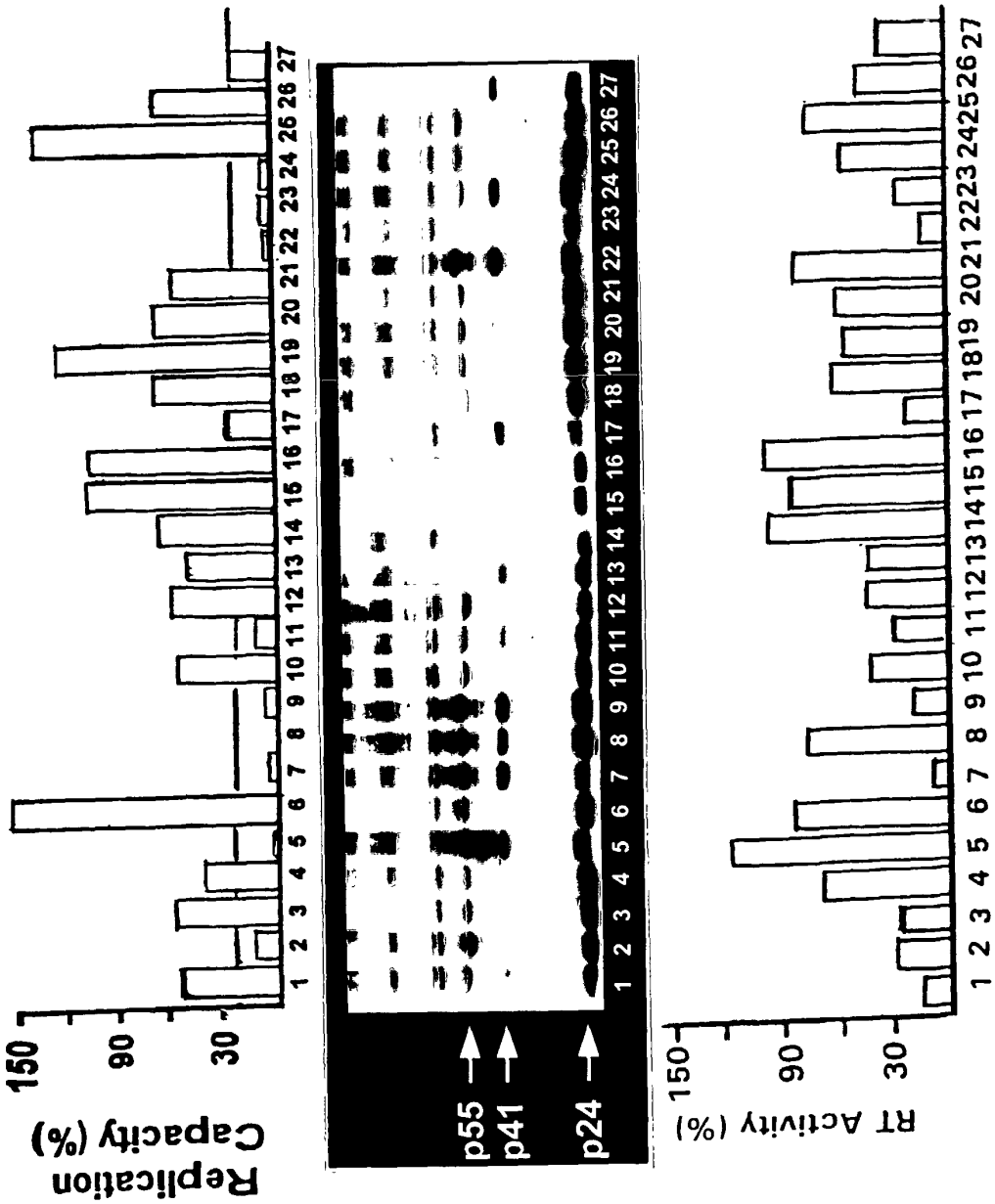


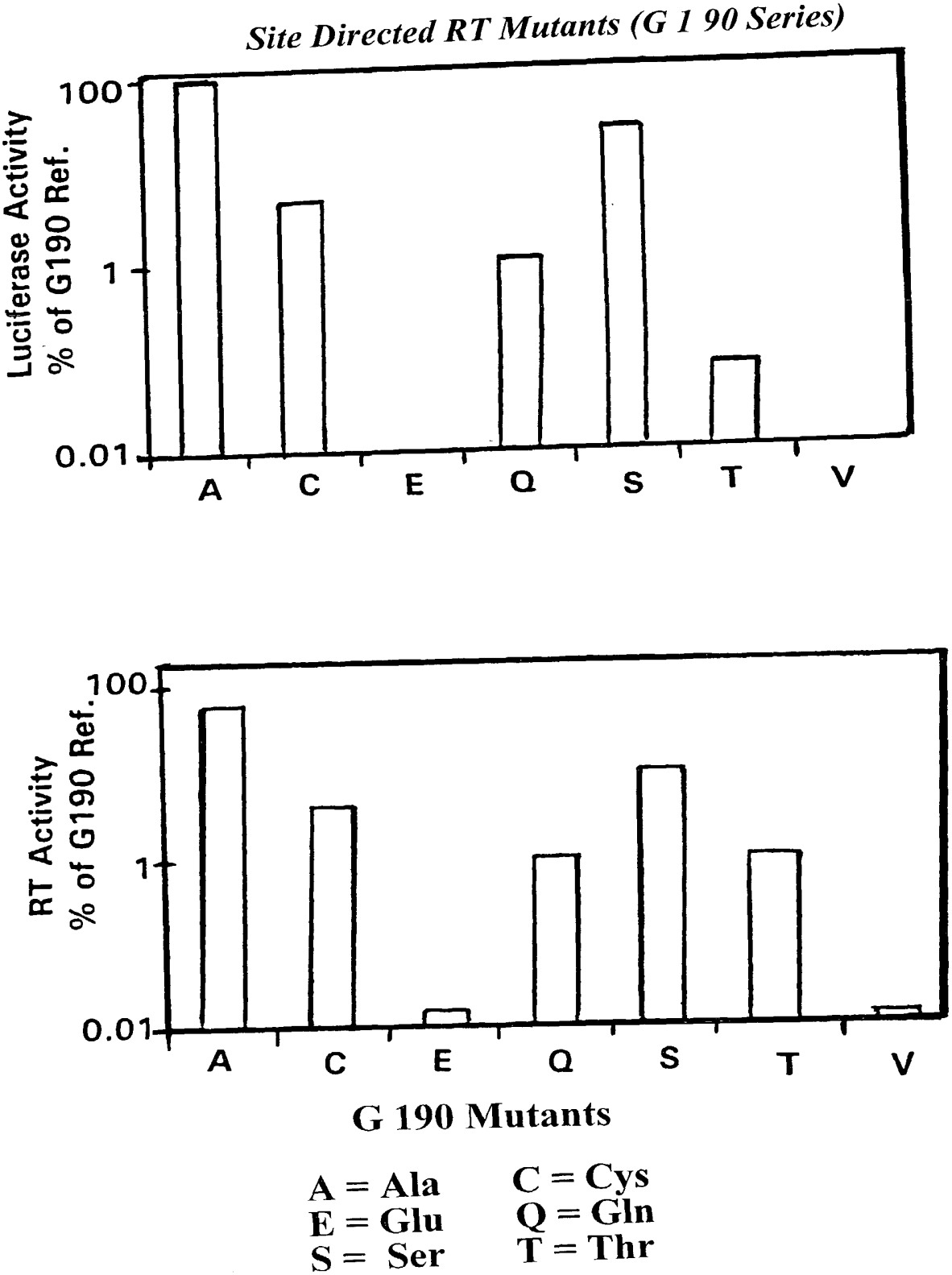
FIGURE 6C

Replication Fitness, PR Processing, and RT Activity



15/50

FIGURE 6D



A = Ala C = Cys
E = Glu Q = Gln
S = Ser T = Thr

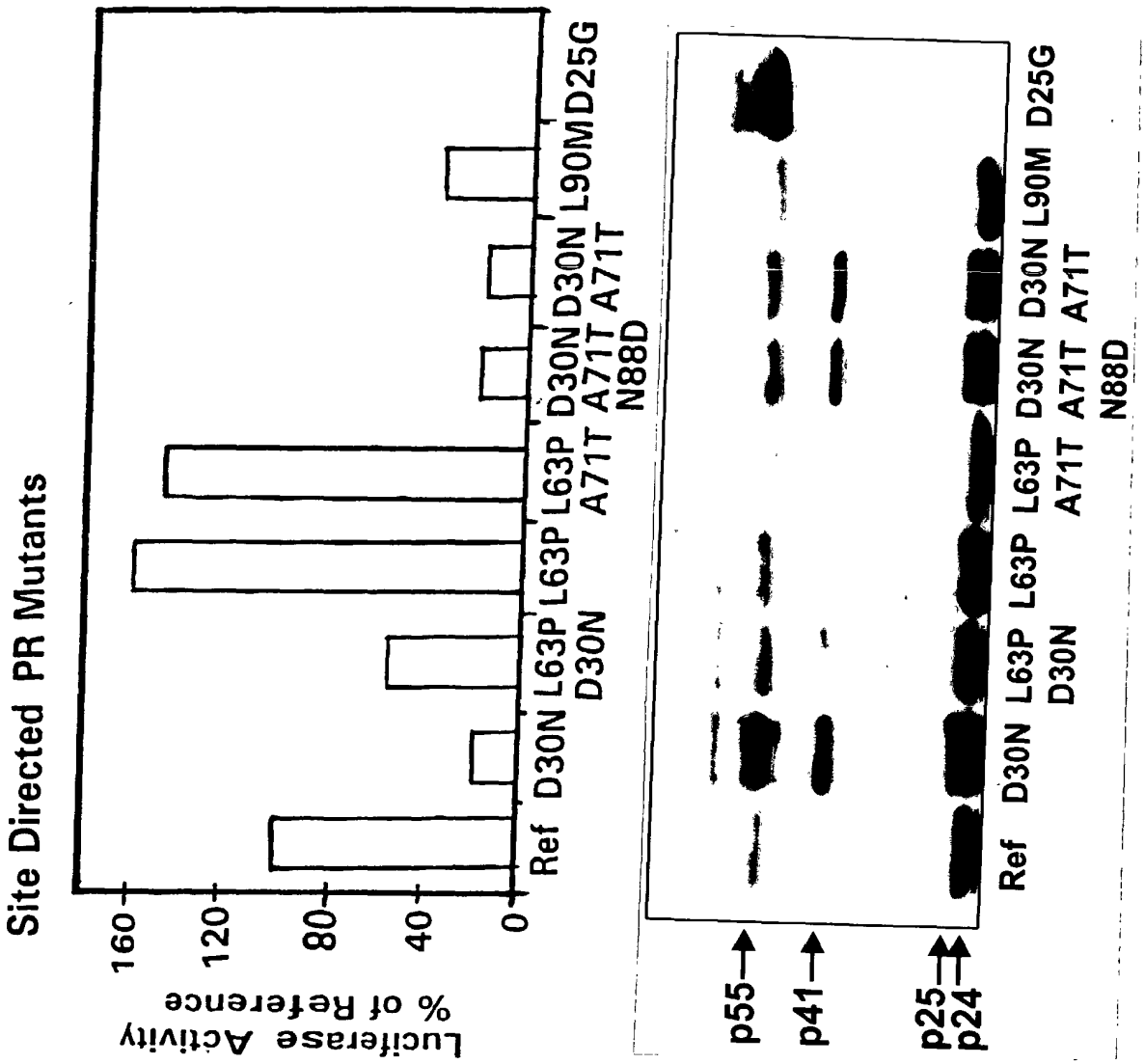


FIGURE 6E

FIGURE 6F

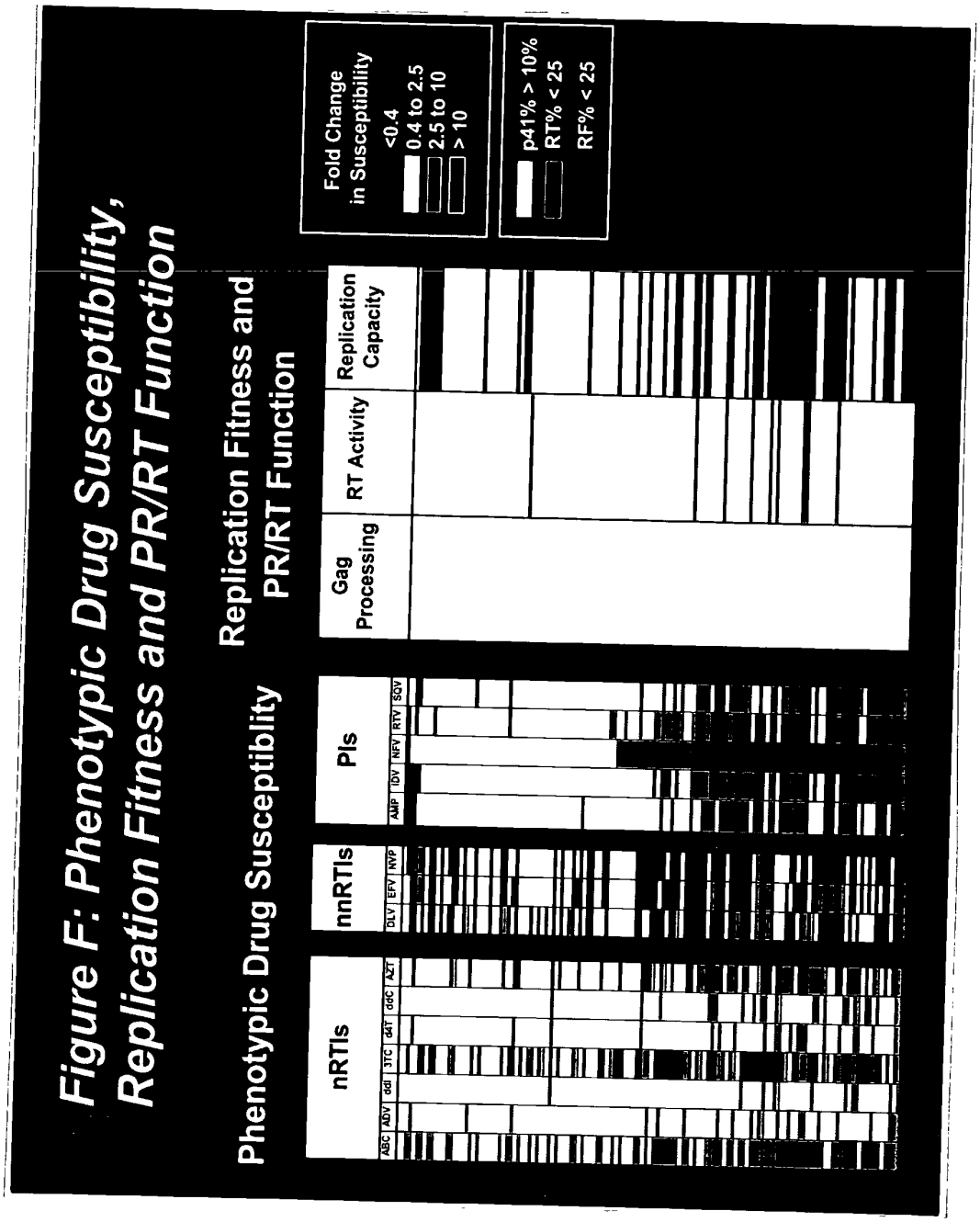
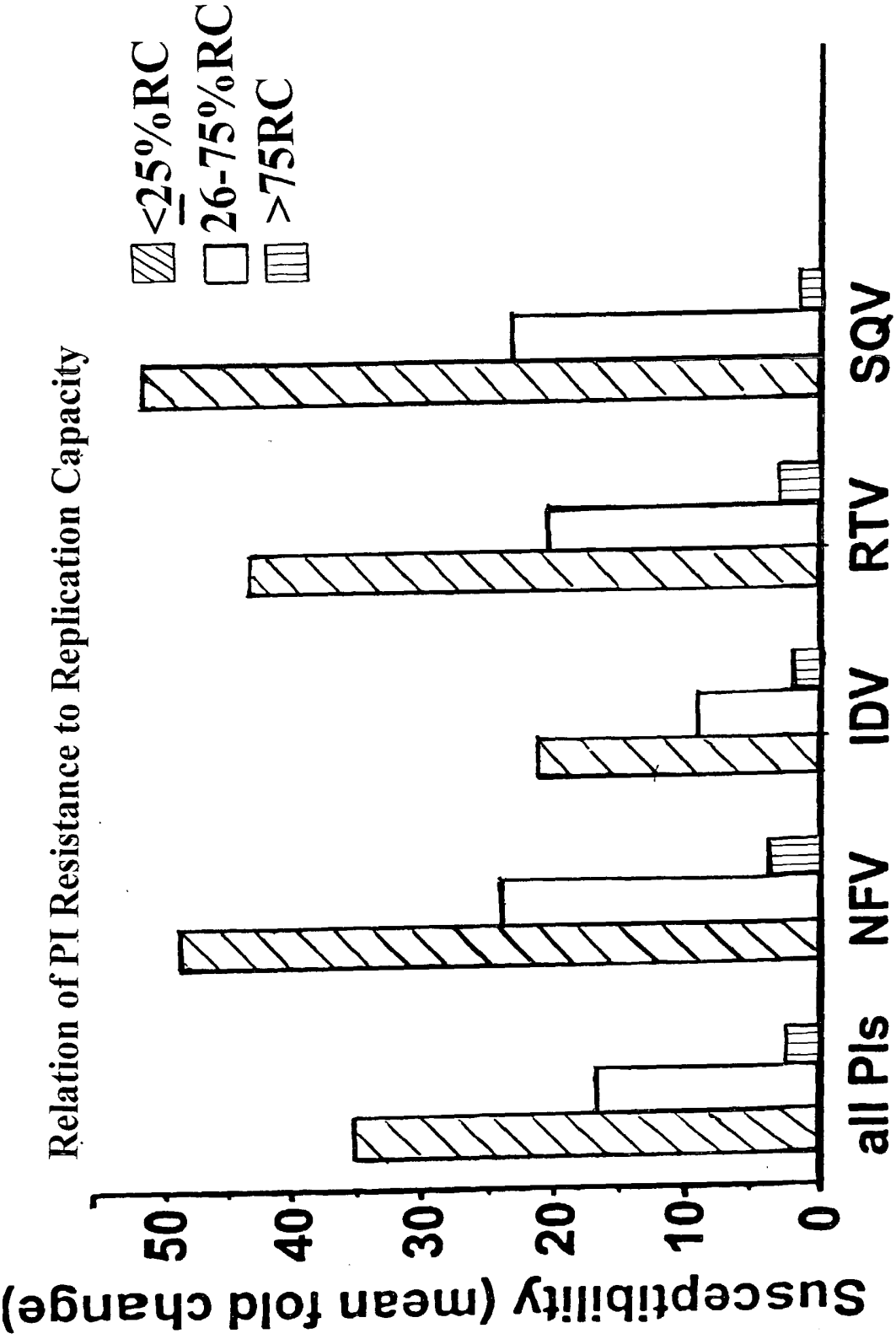


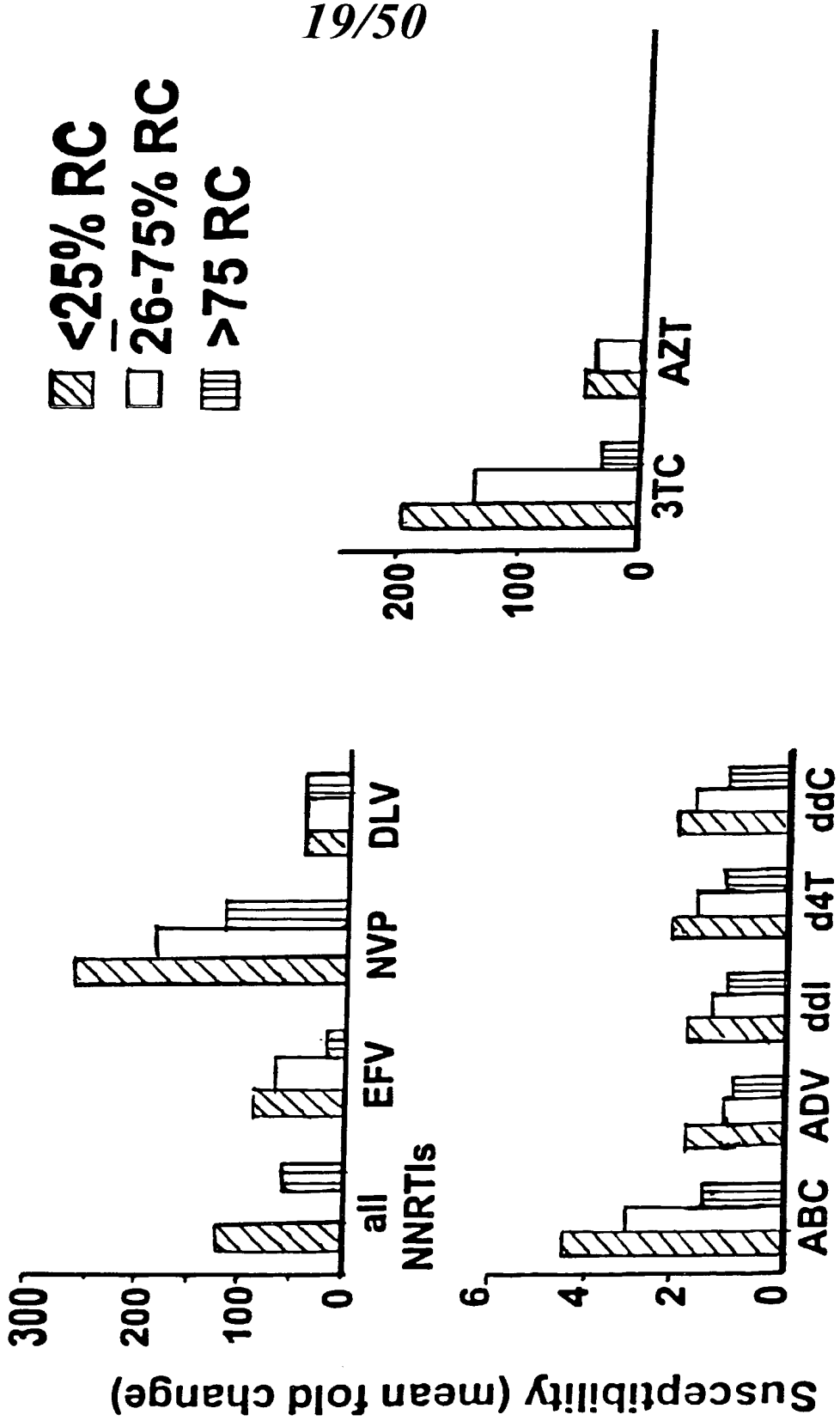
FIGURE 6G



Applicants : Neil T. Parkin and Rainer Ziermann
U. S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 19 of 50

FIGURE 6H

Relation of NRTI and NNRTI Resistance to Replication Capacity



20/50

FIGURE 6I

Low Replication Capacity is Associated with High Numbers of Mutations in Protease and L90M

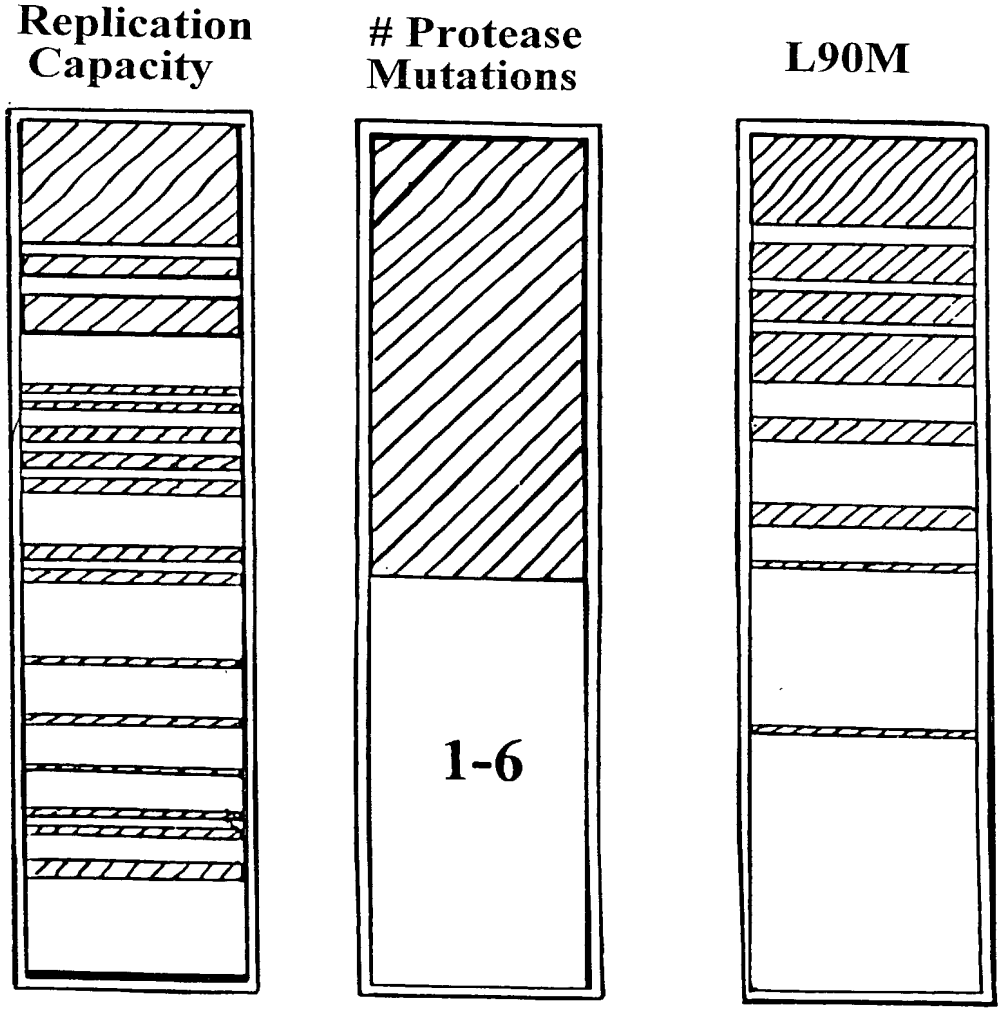
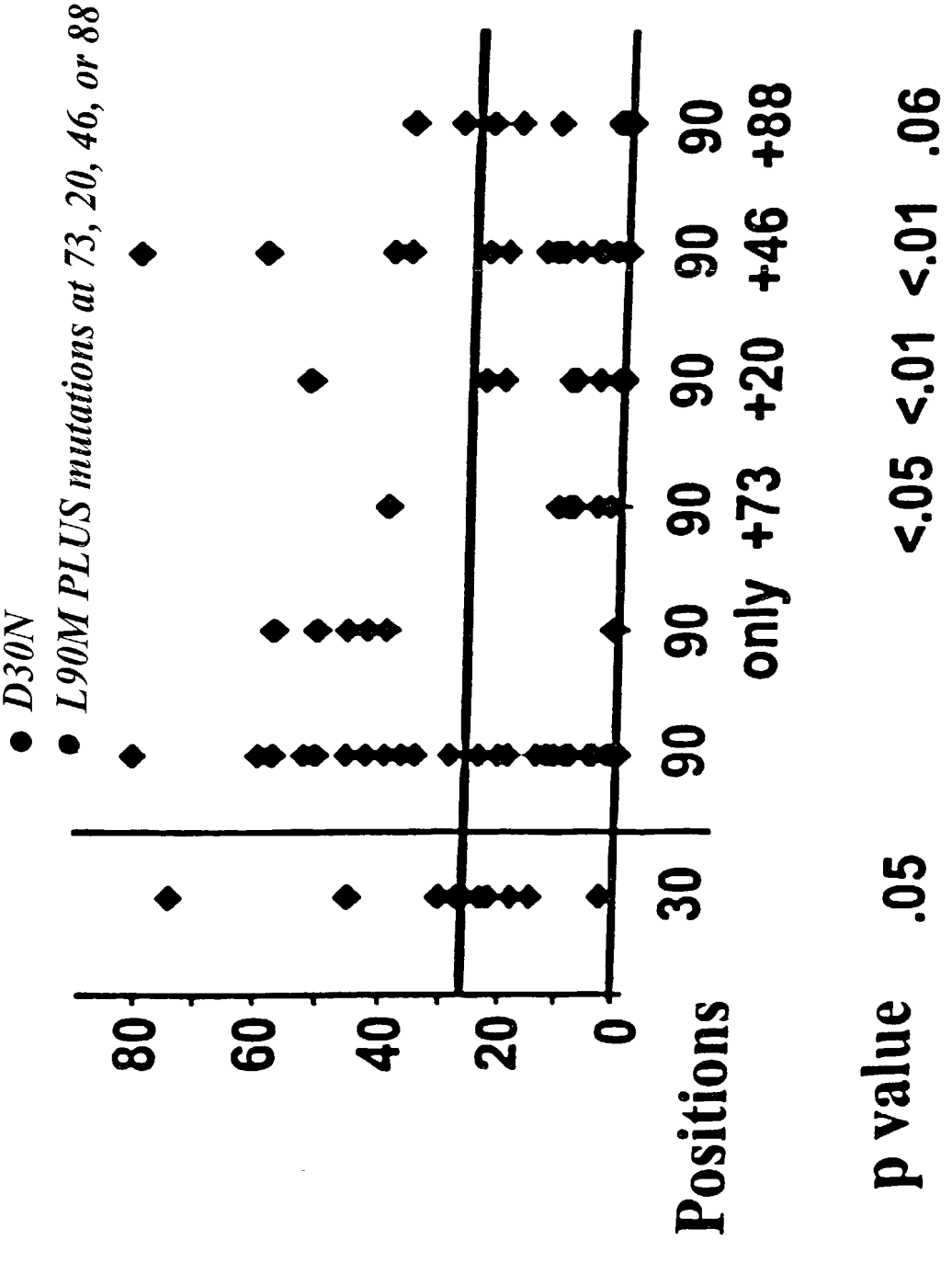


FIGURE 6J

Low Replication Capacity is Associated With Specific Protease Mutations



Relation of NFV Phenotypic Drug Susceptibility, gag Processing and Replication Fitness

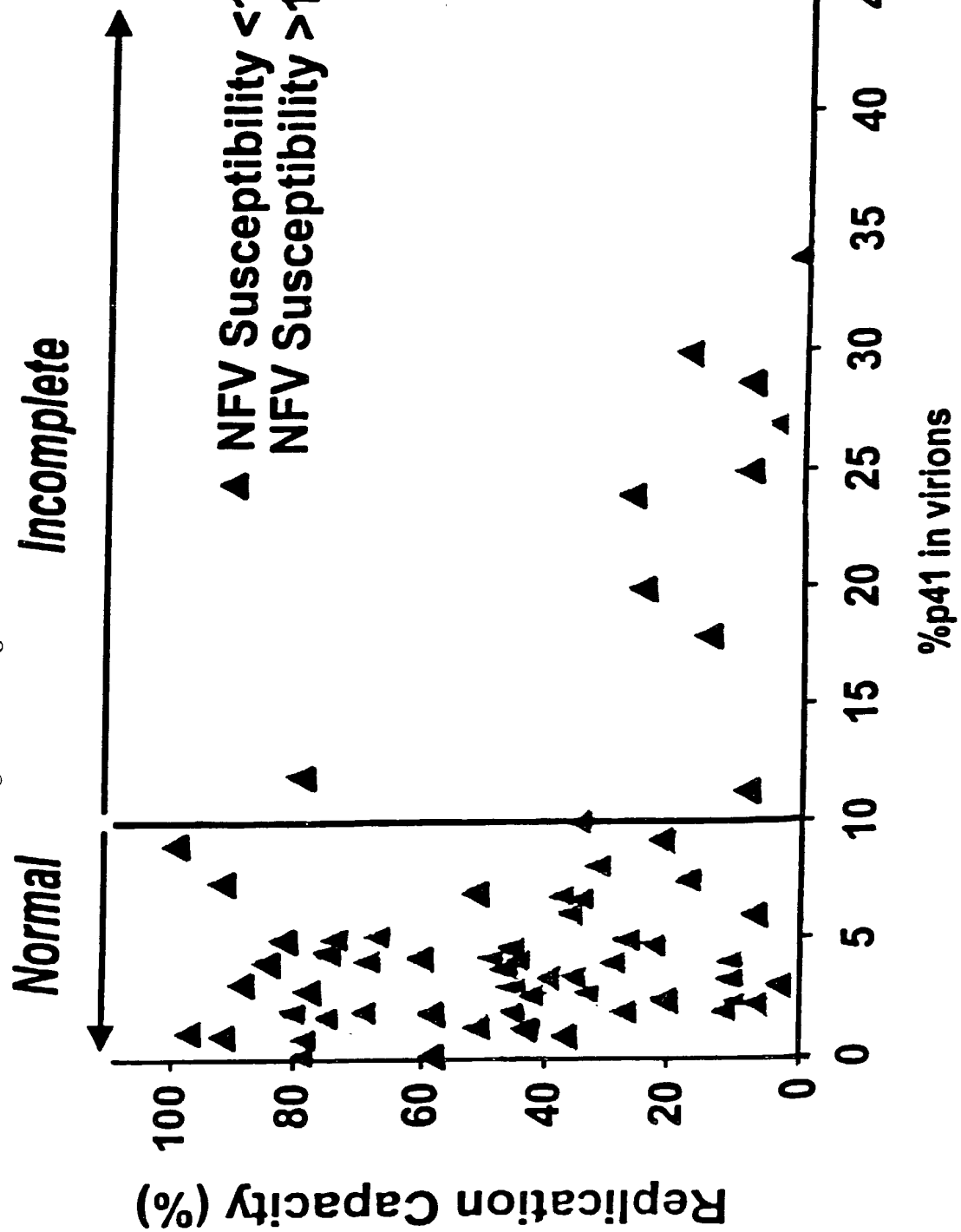


FIGURE 6K

FIGURE 6L

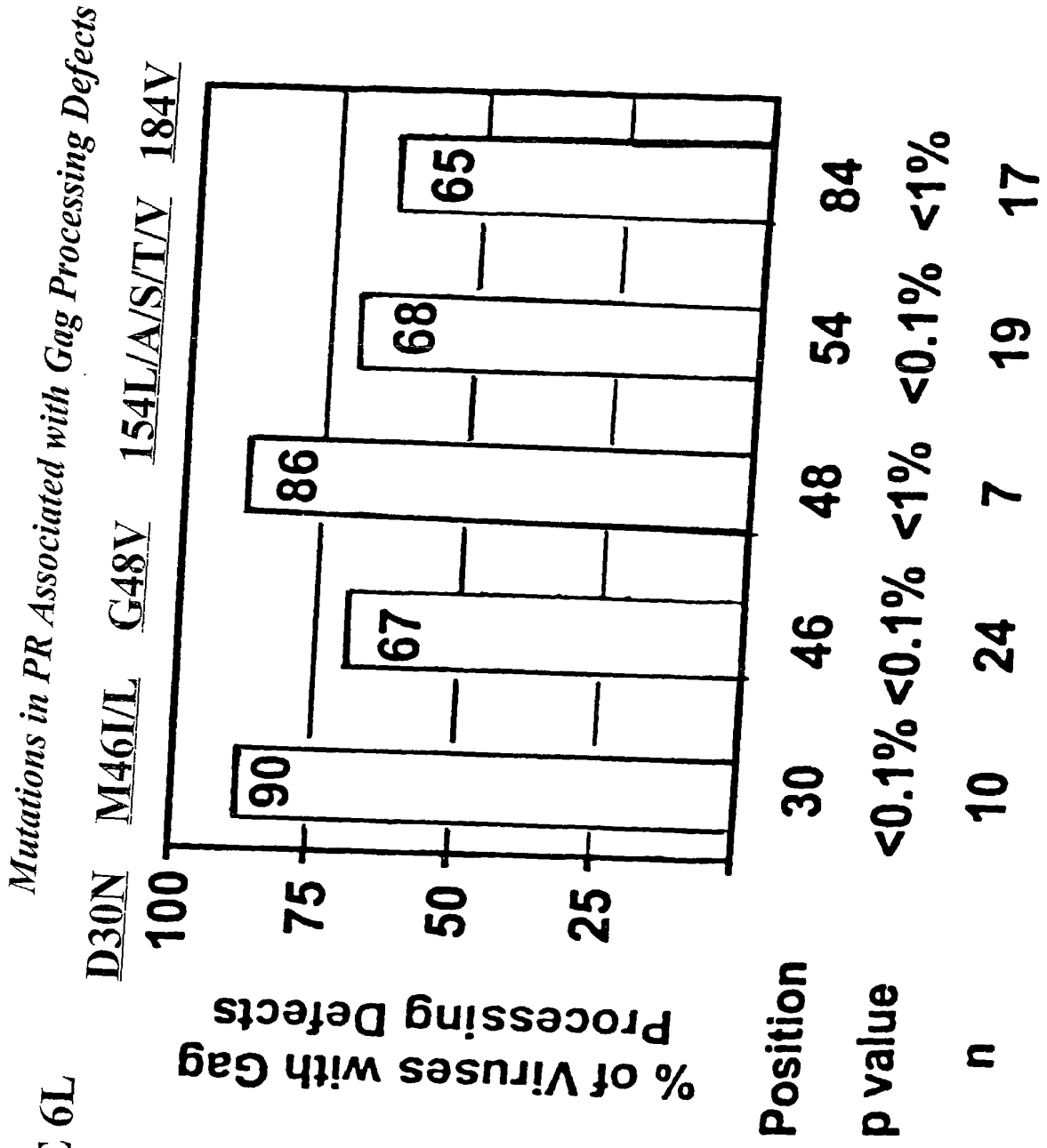


FIGURE 6M

	NRTI				NNRTI			PI				
WEEK	AZT	3TC	D4T	ABC	NVP	DLV	EFV	SQV	IDV	RTV	NFV	AMP
day 0	3.7	>100	2.8	19	>300	88	115	85	72	73	74	16
1	4.5	>100	3.3	20	>300	78	134	95	74	59	80	21
2	5.8	>100	3.2	14	>300	75	142	89	77	49	59	19
3	6.5	>100	2.7	15	>300	96	183	59	75	52	51	15
4	6.3	>100	3.1	15	>300	94	174	59	68	50	49	15
5	6.4	>100	3.0	17	>300	76	119	59	60	54	36	10
6	5.0	>100	2.8	19	>300	93	168	89	39	80	40	18
7	9.1	>100	4.1	12	>300	89	154	85	78	53	53	19
9	2.8	8.1	1.9	5.0	22	15	10	1.8	3.5	4.7	4.0	2.0
10	1.5	1.7	1.1	1.3	1.7	2.0	1.6	0.9	1.6	1.9	1.8	1.6
11	0.9	1.2	1.0	1.2	0.8	1.1	0.9	1.0	1.1	1.1	1.1	1.0
12	0.8	1.3	0.8	1.2	0.5	1.0	0.8	0.8	0.8	0.9	1.1	0.8
23	0.7	1.1	1.0	0.6	0.8	1.1	0.8	0.8	0.8	1.0	0.9	0.6

Patient Virus Reversion to Drug Susceptibility After Treatment Interruption

Applicants : Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 24 of 50

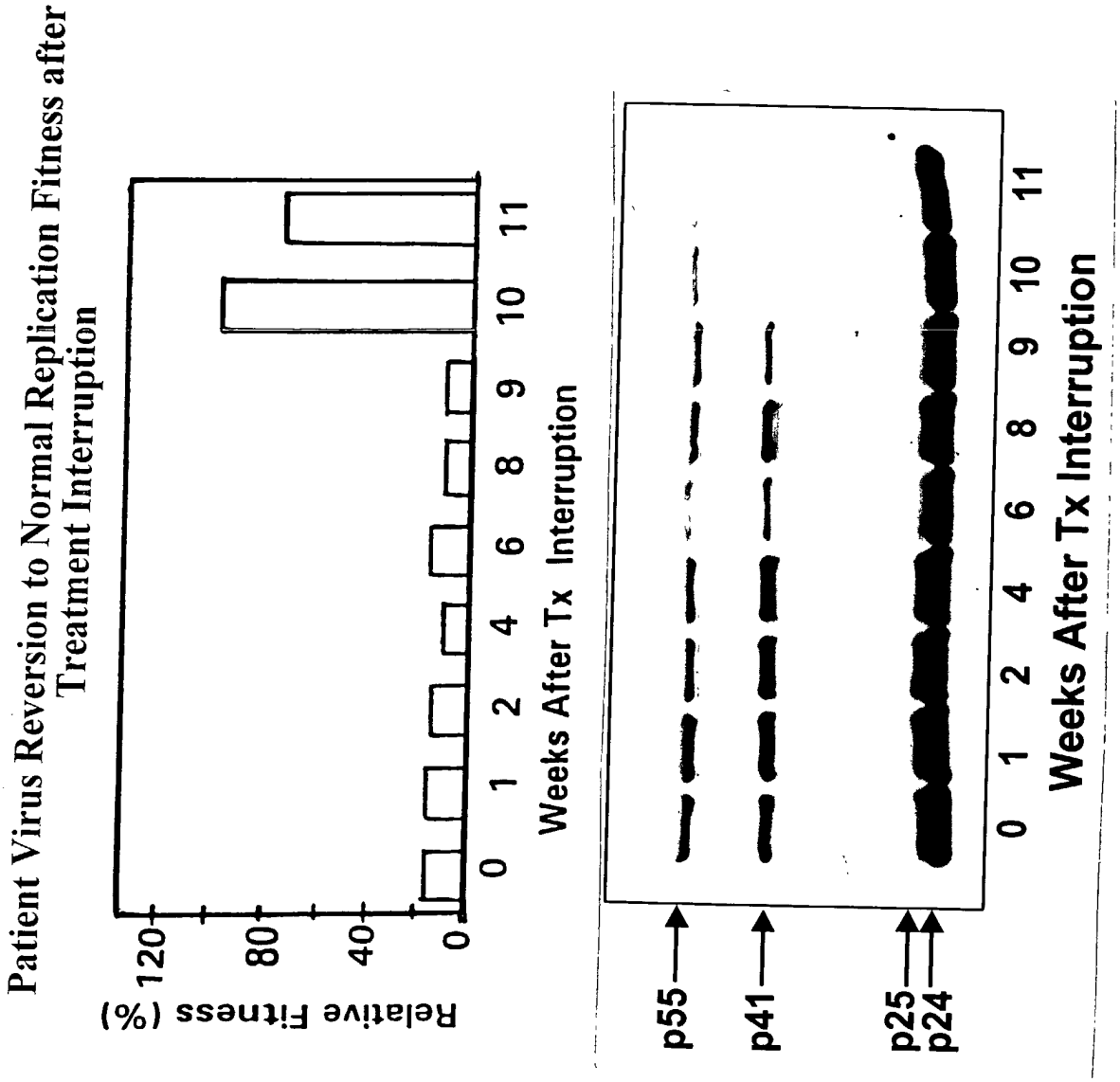
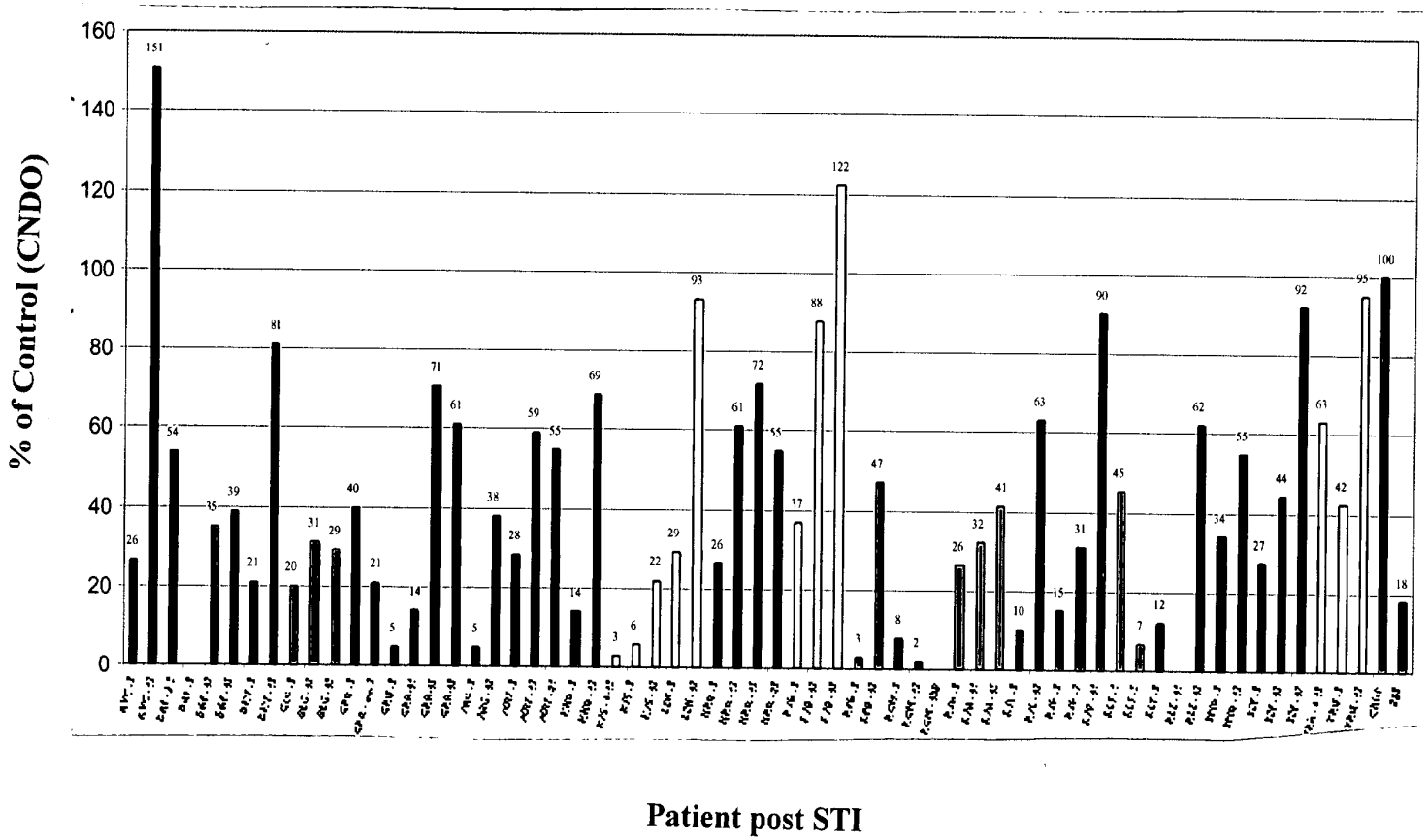


FIGURE 6N

FIGURE 6O

Fitness on GCRC STI Samples (wk 0 and 12)-Assay#2
RLU corrected for p24 input (% of control)



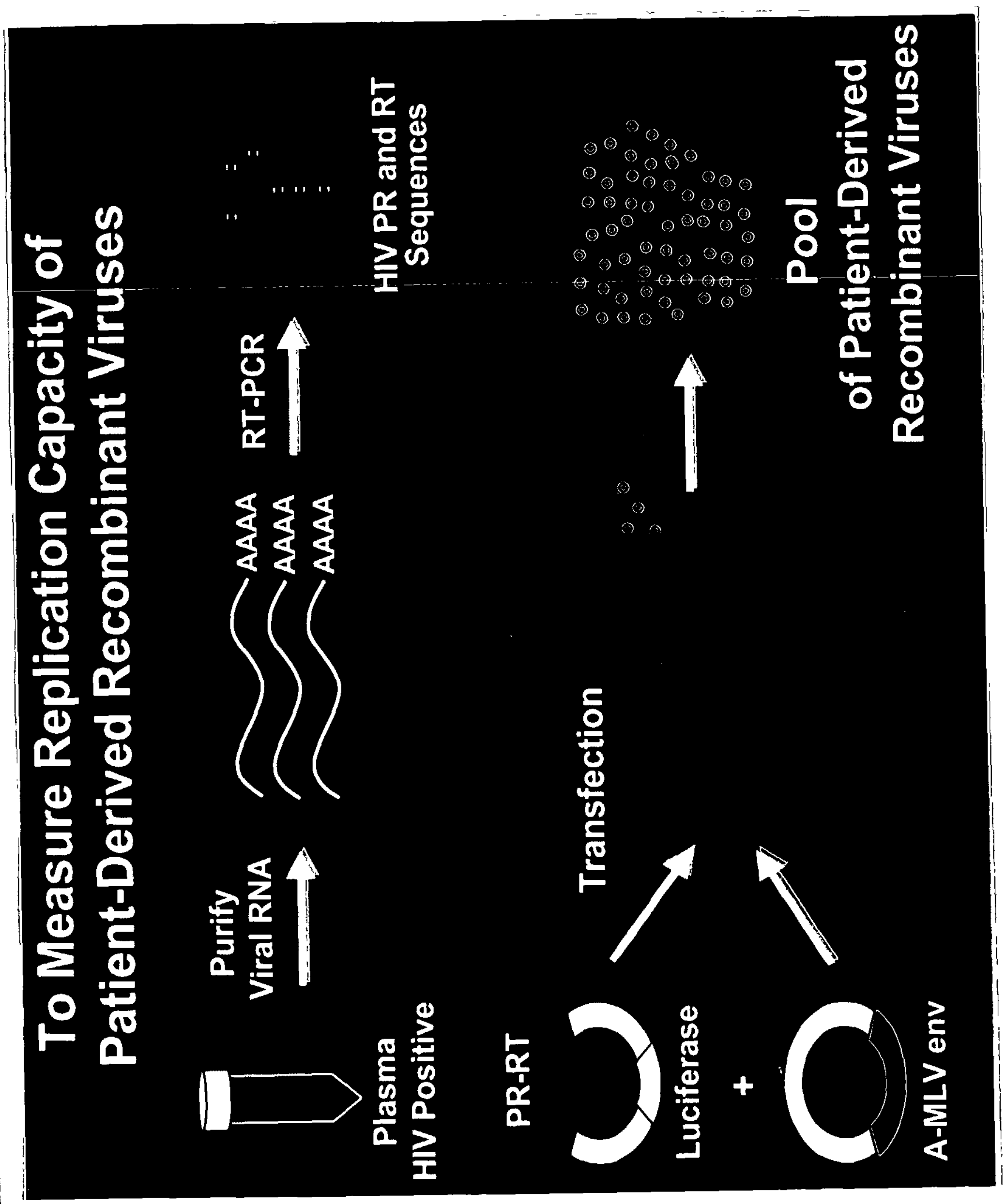


FIGURE 6P

FIGURE 6Q

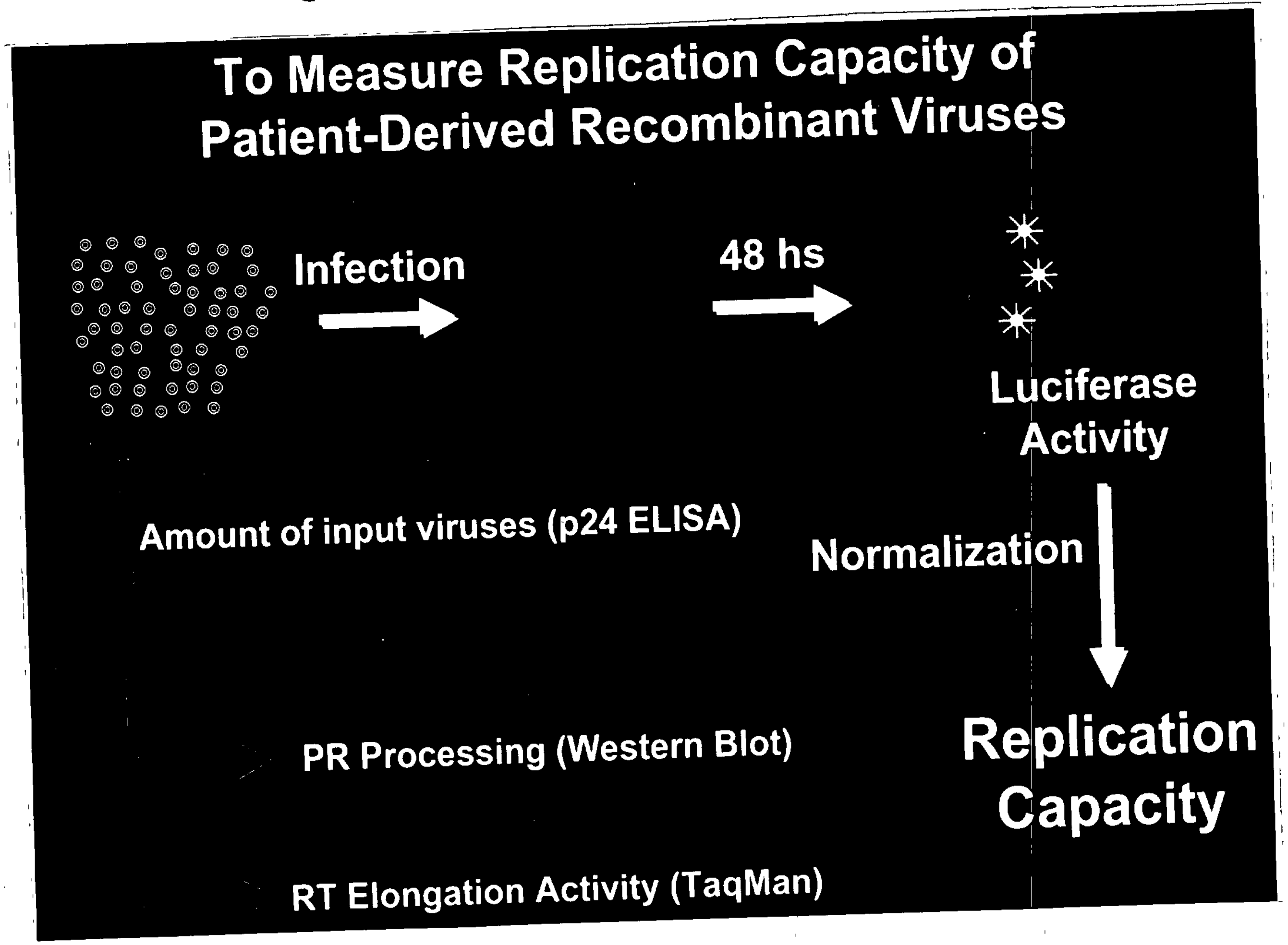
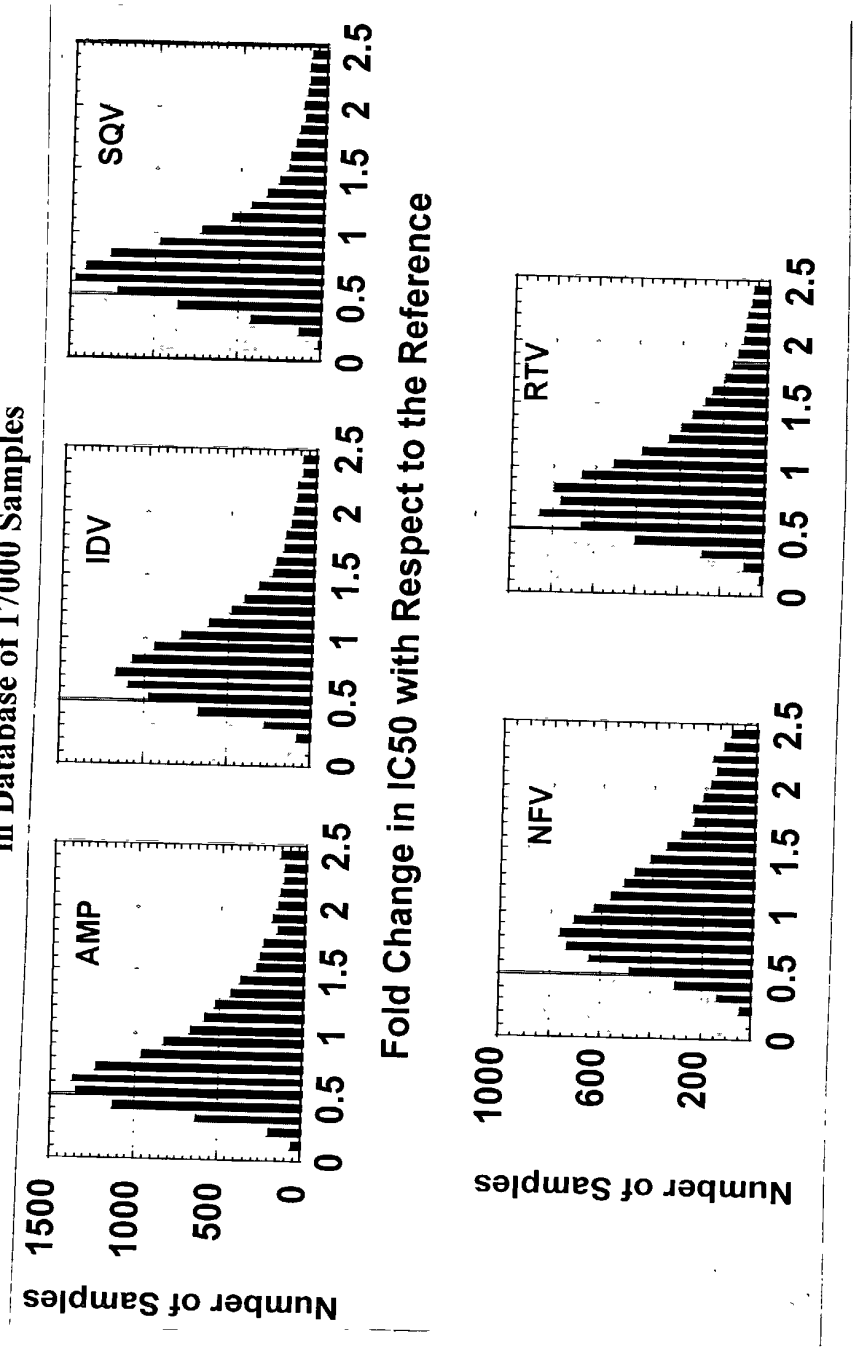


FIGURE 6



Fold Change in IC50 with Respect to the Reference

FIGURE 7

Fold Change Susceptibility
20 Randomly Selected Patient Viruses with HS to PIs

	RT Inhibitors									PR Inhibitors				
Sample	ABC	ddI	3TC	d4T	ddC	ZDV	DLV	EFV	NVP	AMP	IDV	NFV	RTV	SQV
1	3.2	2.2	>300	0.9	1.7	1.2	0.9	41.9	>700	0.4	0.6	1.1	0.4	0.3
2	1.0	1.0	1.3	1.1	1.1	0.7	1.2	0.8	0.8	0.6	0.3	0.7	0.2	0.3
3	3.1	1.7	>300	0.9	nd	0.7	nd	1.1	0.8	0.2	0.4	0.6	0.4	0.3
4	3.3	1.9	>300	1.0	2.4	1.2	62.9	101	429	0.2	0.4	0.6	0.4	0.2
5	3.6	2.2	5.0	1.7	3.2	0.6	>190	>320	>700	0.2	0.4	0.6	0.5	0.3
6	7.5	1.4	>300	1.4	2.1	22.9	12.8	135	>700	0.5	0.5	0.6	0.4	0.4
7	8.5	1.9	>300	3.7	3.4	73.9	30.6	>320	>700	0.3	0.4	0.6	0.3	0.4
8	2.7	1.6	>300	1.0	1.8	1.1	>190	89.3	>700	0.4	0.4	0.5	0.6	0.4
9	2.0	1.1	>300	0.7	1.3	0.8	8.0	72.1	165	0.3	0.4	0.5	0.3	0.5
10	2.4	1.7	>300	1.2	1.9	0.6	71.5	38.7	109	0.4	0.4	0.4	0.4	0.4
11	2.8	1.5	>300	0.7	1.7	0.4	30.9	94.9	193	0.4	0.4	0.4	0.5	0.4
12	3.4	1.1	>300	1.0	2.1	0.7	3.2	2.0	2.6	0.3	0.5	0.4	0.5	0.4
13	3.1	2.1	>300	1.1	3.8	0.6	2.4	1.1	1.5	0.3	0.3	0.4	0.3	0.3
14	1.6	1.1	2.0	0.9	1.5	0.9	>190	60.4	>700	0.2	0.3	0.3	0.2	0.2
15	1.2	1.0	1.2	1.1	1.2	1.7	1.2	1.2	1.2	0.2	0.4	0.3	0.4	0.6
16	2.8	1.3	3.5	1.2	1.2	14.3	21.9	12.4	71.8	0.2	0.3	0.2	0.2	0.4
17	3.0	2.0	>300	1.2	1.8	2.0	11.3	22.1	160	0.2	0.2	0.2	0.2	0.2
18	3.9	1.4	>300	1.6	1.5	3.1	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.3
19	3.1	1.1	49.5	1.6	1.5	6.9	13.4	9.9	33.2	0.3	0.2	0.2	0.2	0.2
20	0.9	1.2	1.3	0.9	0.8	1.0	0.8	0.6	0.6	0.3	0.3	0.2	0.3	0.3

0 - 0.4 | 0.4 - 2.5 | 2.5 - 10 | > 10

Applicants - Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 30 of 50

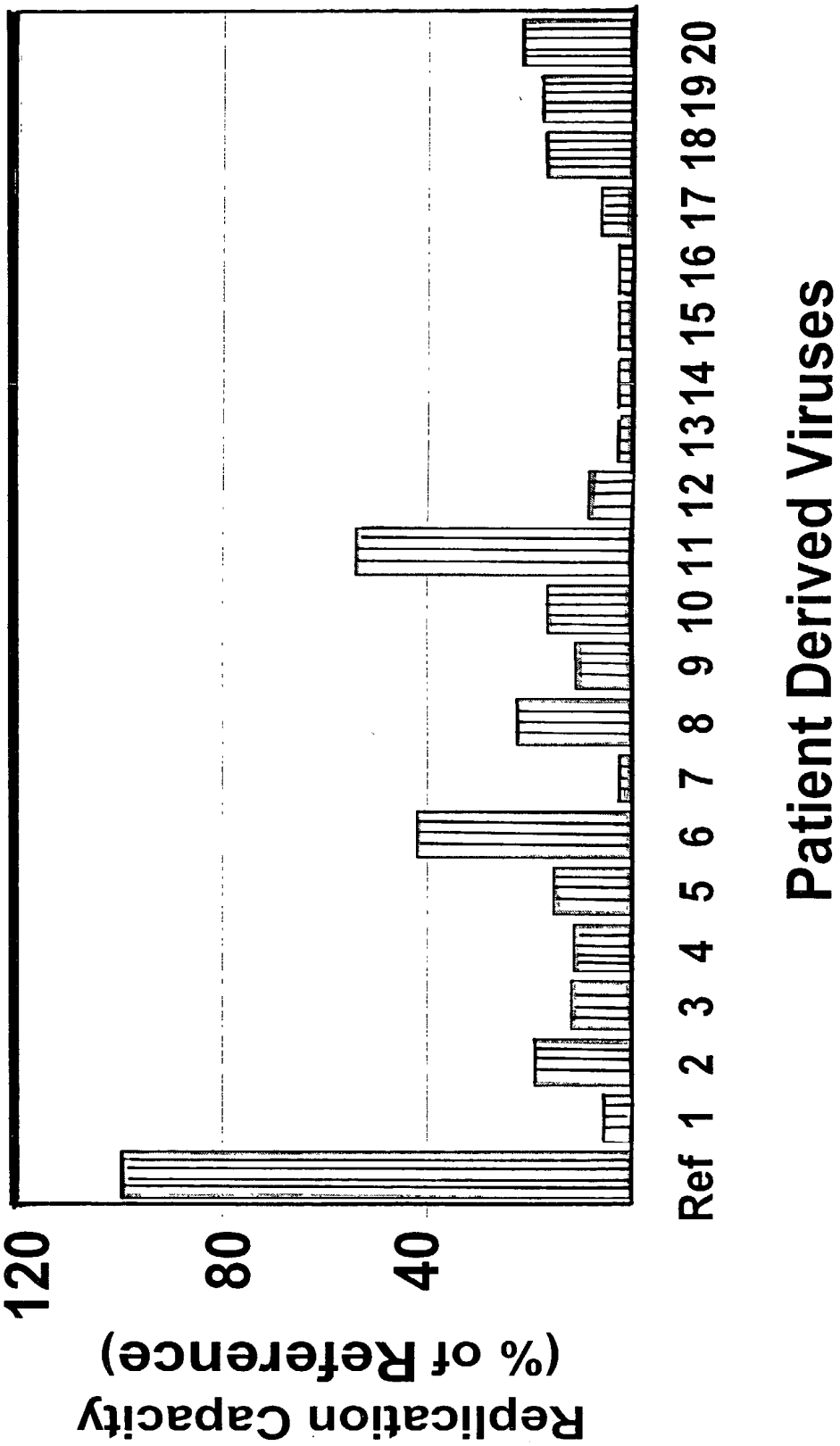
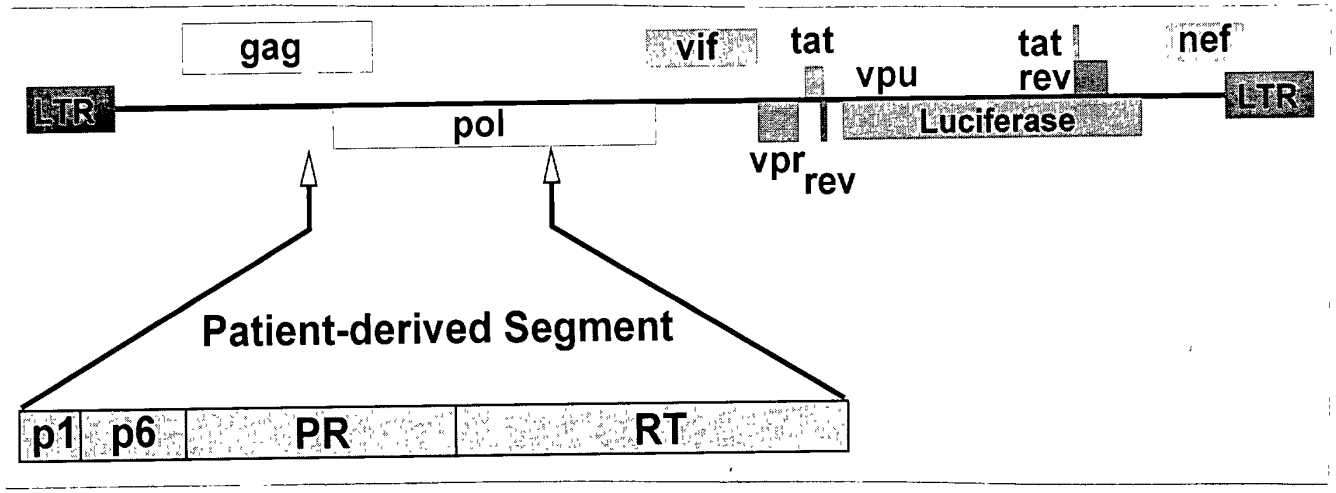


FIGURE 8

FIGURE 9

Cell based assay to measure phenotypic drug susceptibility employimg patient-derived recombinant viruses



Applicants : Neil T. Parkin and Rainer Ziermann
U. S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 32 of 50

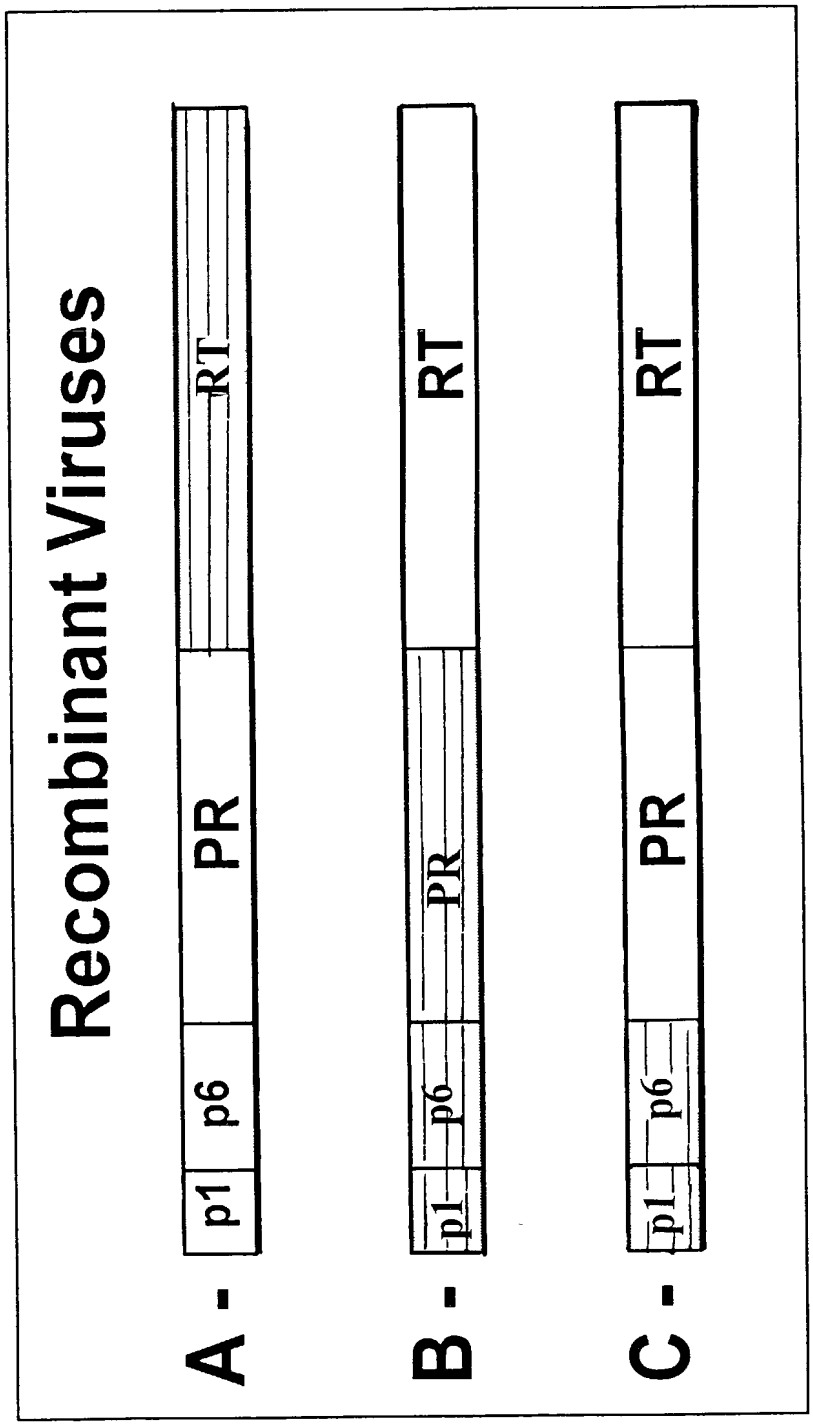
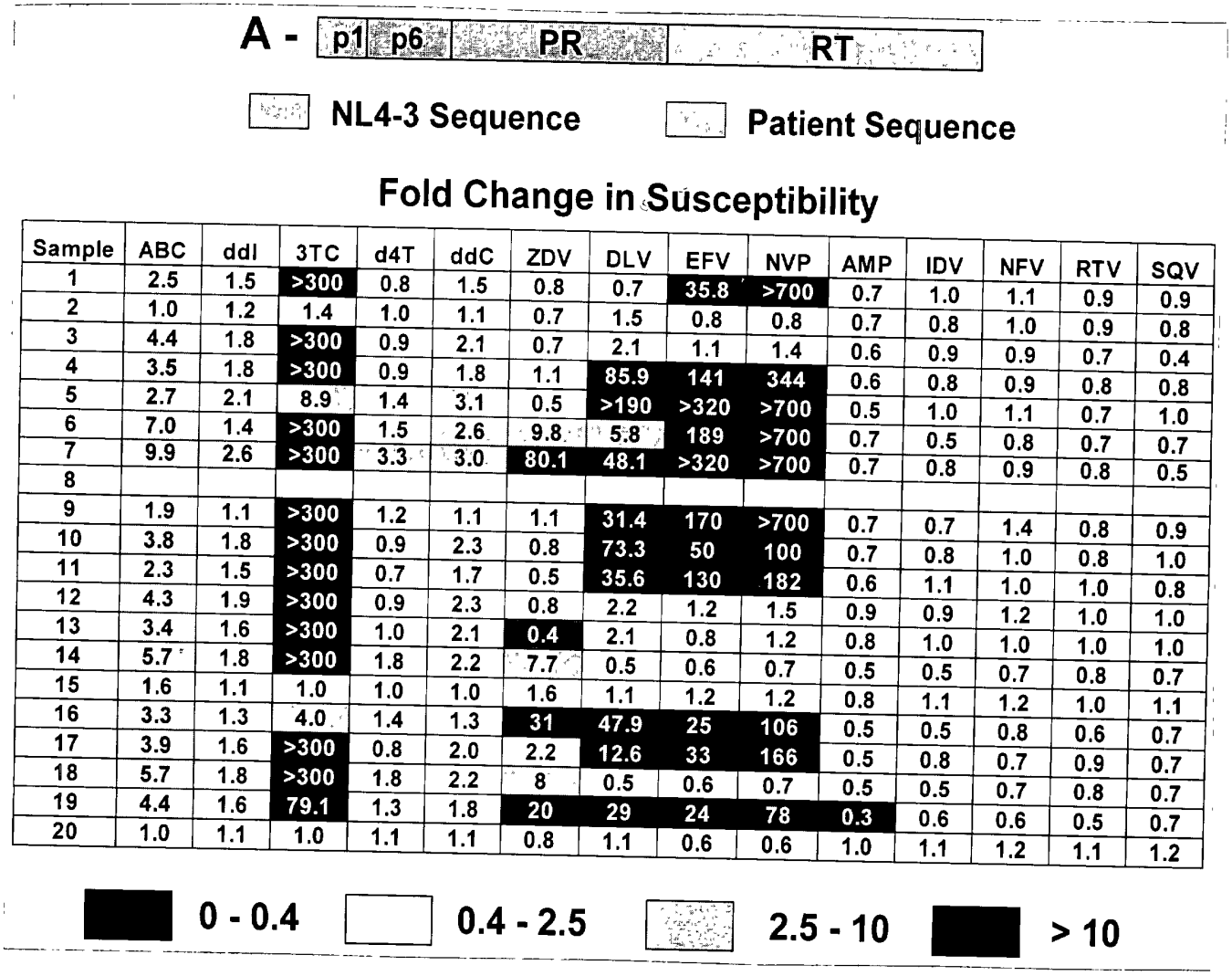


FIGURE 10

Applicants : Neil T. Parkin and Rainer Ziermann
U. S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 34 of 50

FIGURE 11



Fold Change in Susceptibility

Sample	ABC	ddI	3TC	d4T	ddC	ZDV	DLV	EFV	NVP	AMP	IDV	NFV	RTV	SQV
1	2.5	1.5	>300	0.8	1.5	0.8	0.7	35.8	>700	0.7	1.0	1.1	0.9	0.9
2	1.0	1.2	1.4	1.0	1.1	0.7	1.5	0.8	0.8	0.7	0.8	1.0	0.9	0.8
3	4.4	1.8	>300	0.9	2.1	0.7	2.1	1.1	1.4	0.6	0.9	0.9	0.7	0.4
4	3.5	1.8	>300	0.9	1.8	1.1	85.9	141	344	0.6	0.8	0.9	0.8	0.8
5	2.7	2.1	8.9	1.4	3.1	0.5	>190	>320	>700	0.5	1.0	1.1	0.7	1.0
6	7.0	1.4	>300	1.5	2.6	9.8	5.8	189	>700	0.7	0.5	0.8	0.7	0.7
7	9.9	2.6	>300	3.3	3.0	80.1	48.1	>320	>700	0.7	0.8	0.9	0.8	0.5
8														
9	1.9	1.1	>300	1.2	1.1	1.1	31.4	170	>700	0.7	0.7	1.4	0.8	0.9
10	3.8	1.8	>300	0.9	2.3	0.8	73.3	50	100	0.7	0.8	1.0	0.8	1.0
11	2.3	1.5	>300	0.7	1.7	0.5	35.6	130	182	0.6	1.1	1.0	1.0	0.8
12	4.3	1.9	>300	0.9	2.3	0.8	2.2	1.2	1.5	0.9	0.9	1.2	1.0	1.0
13	3.4	1.6	>300	1.0	2.1	0.4	2.1	0.8	1.2	0.8	1.0	1.0	1.0	1.0
14	5.7	1.8	>300	1.8	2.2	7.7	0.5	0.6	0.7	0.5	0.5	0.7	0.8	0.7
15	1.6	1.1	1.0	1.0	1.0	1.6	1.1	1.2	1.2	0.8	1.1	1.2	1.0	1.1
16	3.3	1.3	4.0	1.4	1.3	31	47.9	25	106	0.5	0.5	0.8	0.6	0.7
17	3.9	1.6	>300	0.8	2.0	2.2	12.6	33	166	0.5	0.8	0.7	0.9	0.7
18	5.7	1.8	>300	1.8	2.2	8	0.5	0.6	0.7	0.5	0.5	0.7	0.8	0.7
19	4.4	1.6	79.1	1.3	1.8	20	29	24	78	0.3	0.6	0.6	0.5	0.7
20	1.0	1.1	1.0	1.1	1.1	0.8	1.1	0.6	0.6	1.0	1.1	1.2	1.1	1.2

0 - 0.4 | 0.4 - 2.5 | 2.5 - 10 | > 10

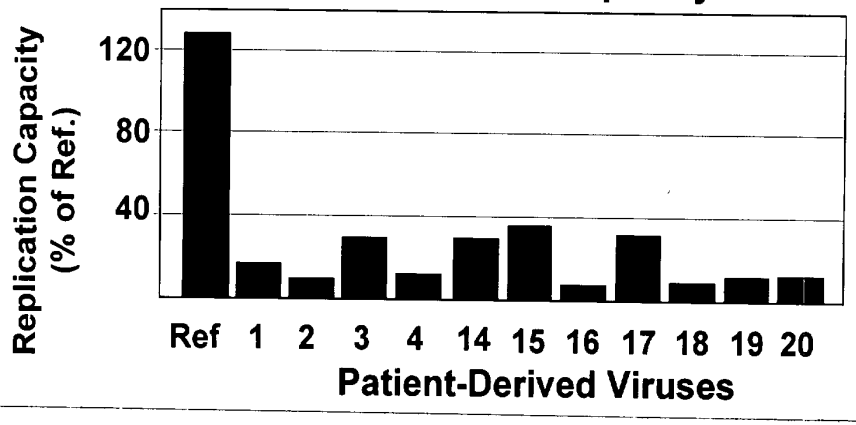
FIGURE 12

NL4-3 Sequence Patient Sequence

Fold Change in Susceptibility

Sample	ABC	ddI	3TC	d4T	ddC	AZT	DLV	EFV	NVP	AMP	IDV	NFV	RTV	SQV
1	0.9	0.9	1.0	1.0	0.9	0.8	0.7	0.8	0.8	0.4	0.6	1.3	0.7	0.5
2	1.0	1.0	1.0	0.9	1.1	1.1	0.6	0.7	0.7	0.6	0.3	0.6	0.2	0.2
3	0.8	1.0	1.0	1.0	0.9	0.9	0.6	0.7	0.6	0.3	0.7	0.7	0.4	0.5
4	0.9	0.9	0.7	1.2	0.9	0.9	0.7	0.8	0.9	0.3	0.5	0.7	0.4	0.4
14	0.9	1.0	1.0	0.9	0.9	0.7	0.7	0.9	0.5	0.3	0.5	0.6	0.7	0.9
15	0.9	1.1	0.9	1.1	1.0	1.1	0.9	0.9	0.7	0.2	0.3	0.3	0.3	0.6
16	0.8	1.0	0.8	1.1	1.1	0.7	0.5	0.8	0.7	0.4	0.3	0.3	0.4	0.5
17	1.0	1.0	0.9	1.0	1.0	1.0	0.7	1.0	0.8	0.2	0.4	0.5	0.4	0.6
18	0.9	0.7	0.8	0.9	0.9	0.9	0.6	0.9	0.5	0.3	0.4	0.4	0.4	0.5
19	0.9	1.0	0.9	0.8	1.0	0.8	0.7	0.9	0.8	0.4	0.4	0.4	0.3	0.6
20	0.9	1.0	1.0	0.9	0.9	1.0	0.6	0.9	0.6	0.2	0.3	0.3	0.3	0.4

Replication Capacity



Applicants : Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 35 of 50

FIGURE 13

NL4-3 Sequence Patient Sequence

Fold Change in Susceptibility

Sample	ABC	ddI	3TC	d4T	ddC	ZDV	DLV	EFV	NVP	AMP	IDV	NFV	RTV	SQV
4	0.9	1.0	0.9	0.9	0.7	0.8	1.1	0.7	0.6	0.6	0.5	0.6	0.6	0.4
15	0.9	1.1	1.0	1.0	0.9	0.8	1.6	0.8	0.8	0.5	0.4	0.4	0.4	0.3
16	0.8	1.0	0.9	1.0	0.9	0.8	1.3	0.7	0.6	0.3	0.4	0.3	0.3	0.5
18	0.9	0.9	1.0	1.0	0.8	0.7	1.1	0.7	0.5	0.2	0.4	0.2	0.2	0.7
19	1.0	1.0	1.0	1.0	0.9	0.7	1.1	0.7	0.5	0.3	0.3	0.3	0.3	0.5

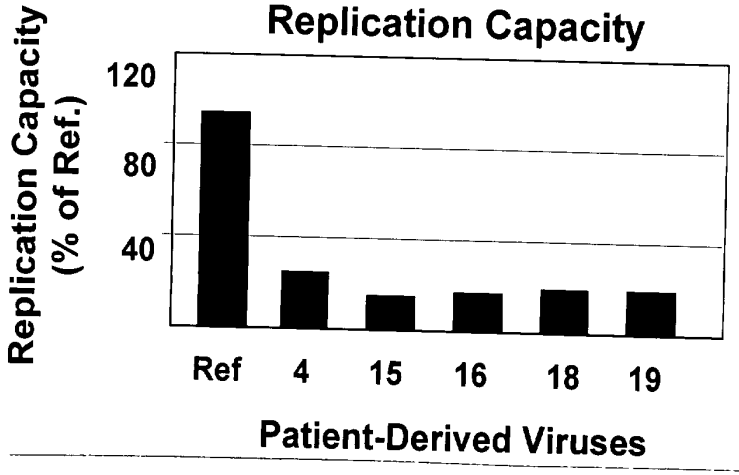


FIGURE 14

What Is the Role of Sequences Flanking the N-Terminus of PR?

1. The Gag Frame Encodes p1 and p6

- p6 contains the L domain (PTAPP) which is critical for virus release from the cell
- p6 is required for proper incorporation of Vpr into the virions as well as retention of pol proteins
- p6 associates with TRiC (chaperonin)

2. The Pol Frame Encodes a Transframe Protein (TFR)

TFR includes a conserved octapeptide (TFP) and p6*

- The TFP is a potent competitive inhibitor of PR in vitro
- p6* modulates PR activity

Applicants : Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 37 of 50

FIGURE 15

Contains Sequences and Structures Required for Frameshift
Slippery heptamer sequence (U UUU UUA)
Stem loop structure downstream of the frameshift site

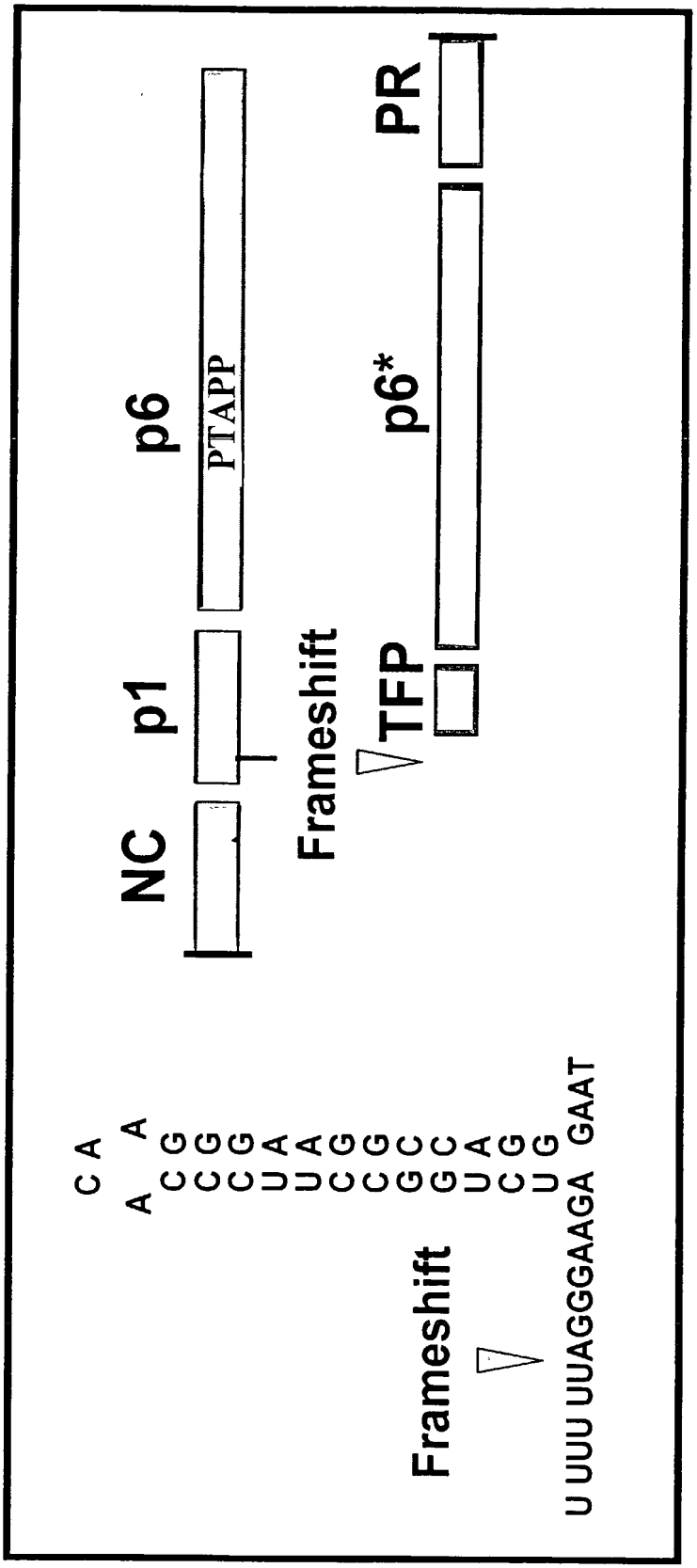


FIGURE 16

Gag p1 and p6

Genotype of Patient-Derived Sequences

```
      ANFLGKIWPSHKGRPGNFLQSRPEPTAPPEESFRFGEETTTPSQKQEPIDKELYPLASLRSLFGNDPSSQ

I     ..........S.........N.....................A......G........ST............
II    ...................V......S...A.....................T...........K.......L..
III   ......L.............N.T.....................-.P.TR.Q.......VT..K.......L..
IV    ..........RS..........................G.....................K..........
```

Transframe Protein

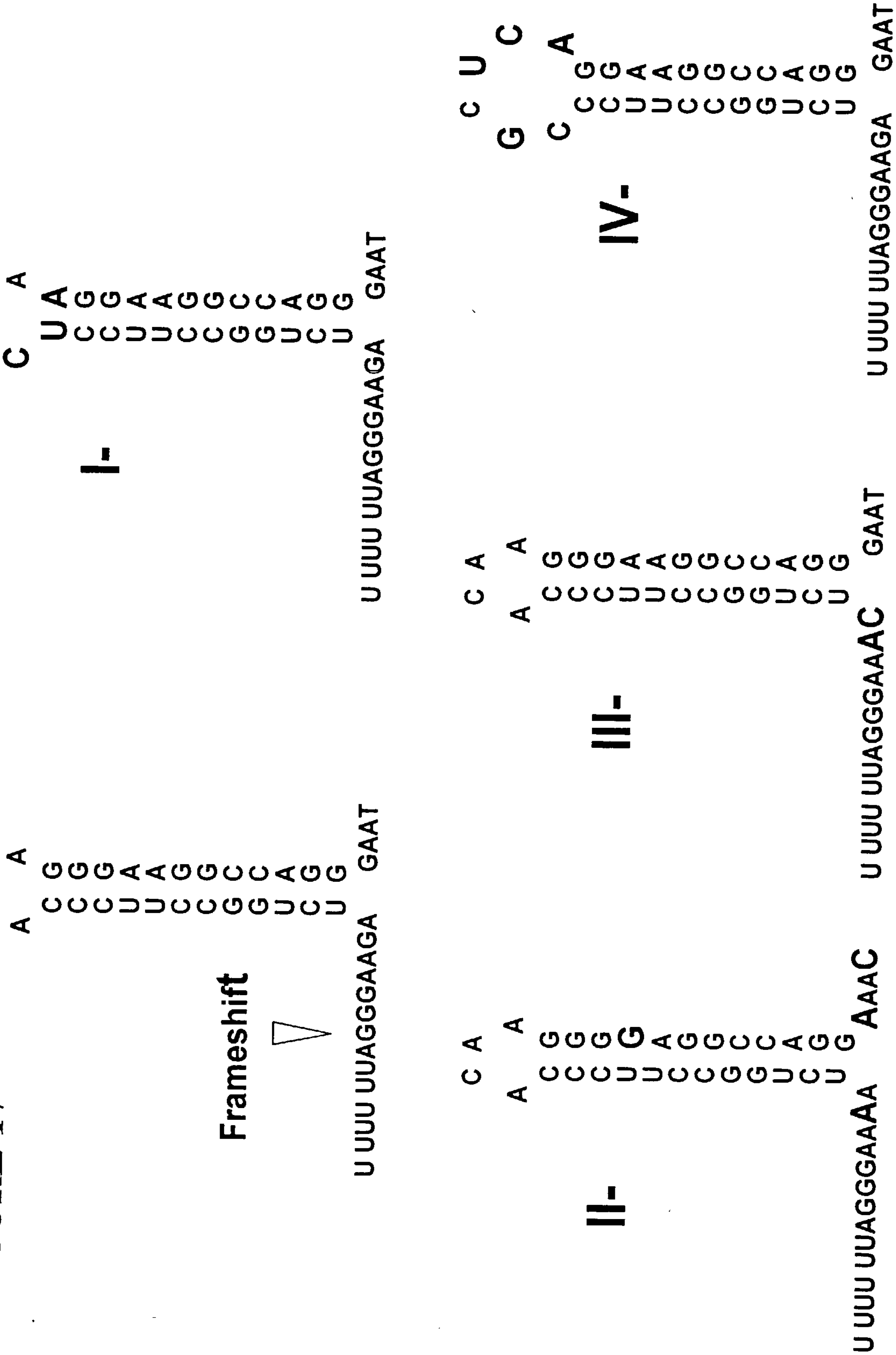
```
      FFREDLAFPQ GKAREFSSEQ TRANSPTRRE LQVWGRDNNS LSEAGADRQT VSFSF

I     ........L. R.........  ..........  .......S..  ......N...  ...NL
II    ....N.....  .E..KLC...  ..TI...S..  ..........  .....D....  .....
III   ....T.....  ......P...  N.......G.  .........-.  P.D......I  ..CN.
IV    ....N....L R.........  ..........  ..........  .....T....  .....
```

* I to IV represent clones derived from patient sample pools that retained the HS to PI

Applicants : Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 39 of 50

FIGURE 17

RNA Sequence of Frameshift Region



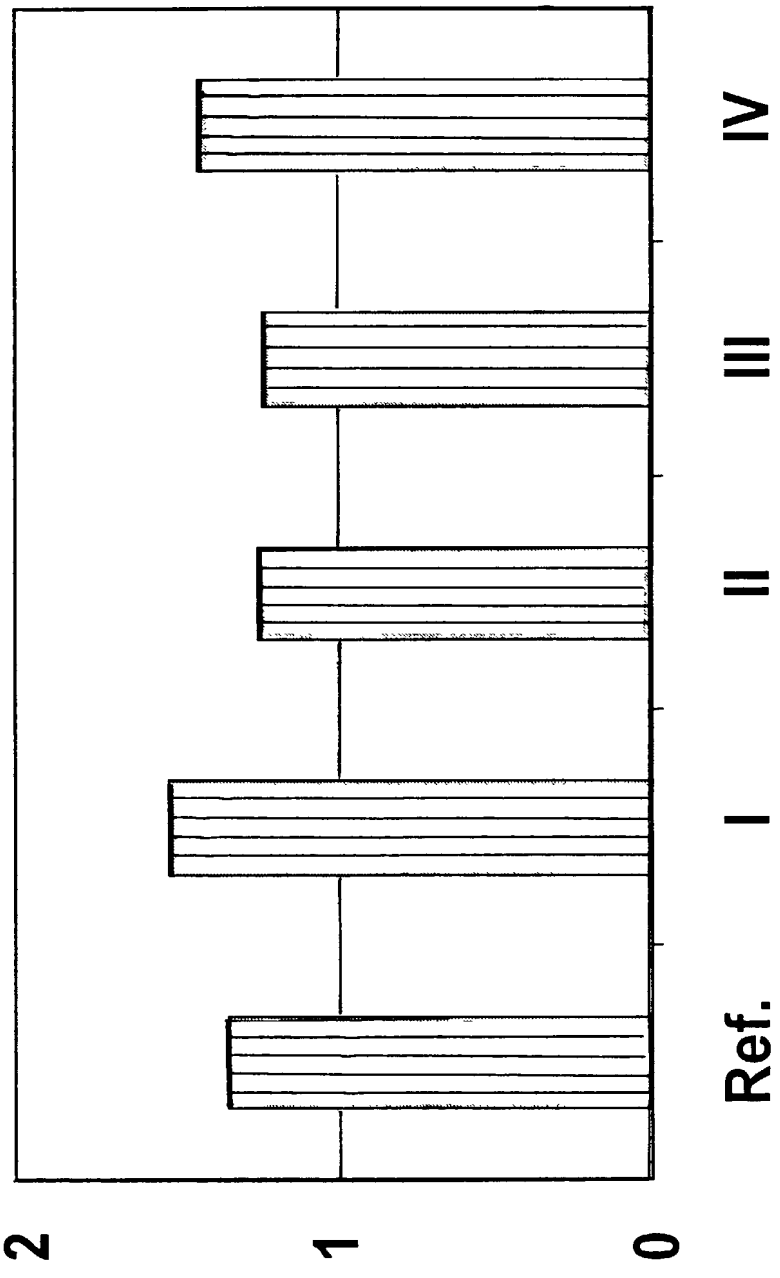


FIGURE 18

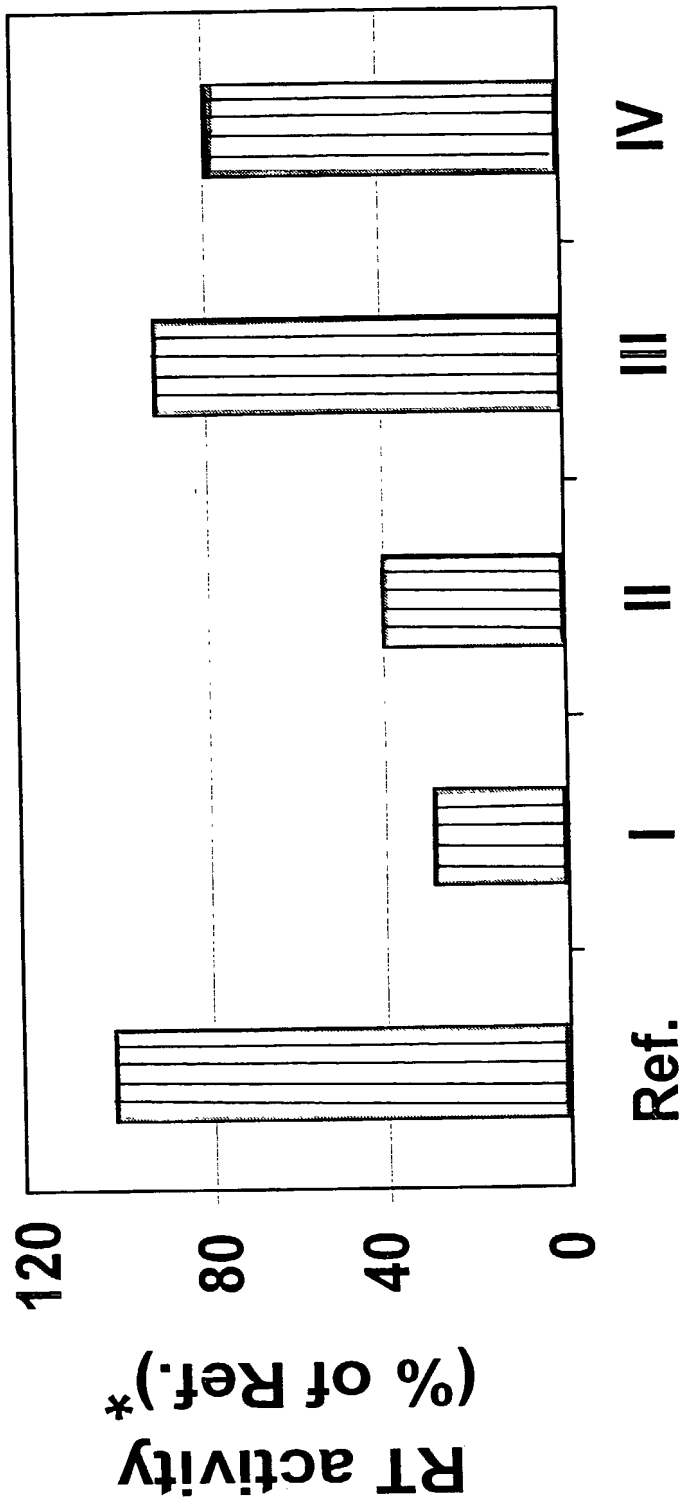


FIGURE 19

FIGURE 20

Processing of Pr55Gag in Virions
Western Blot analysis using anti-p24 antibodies

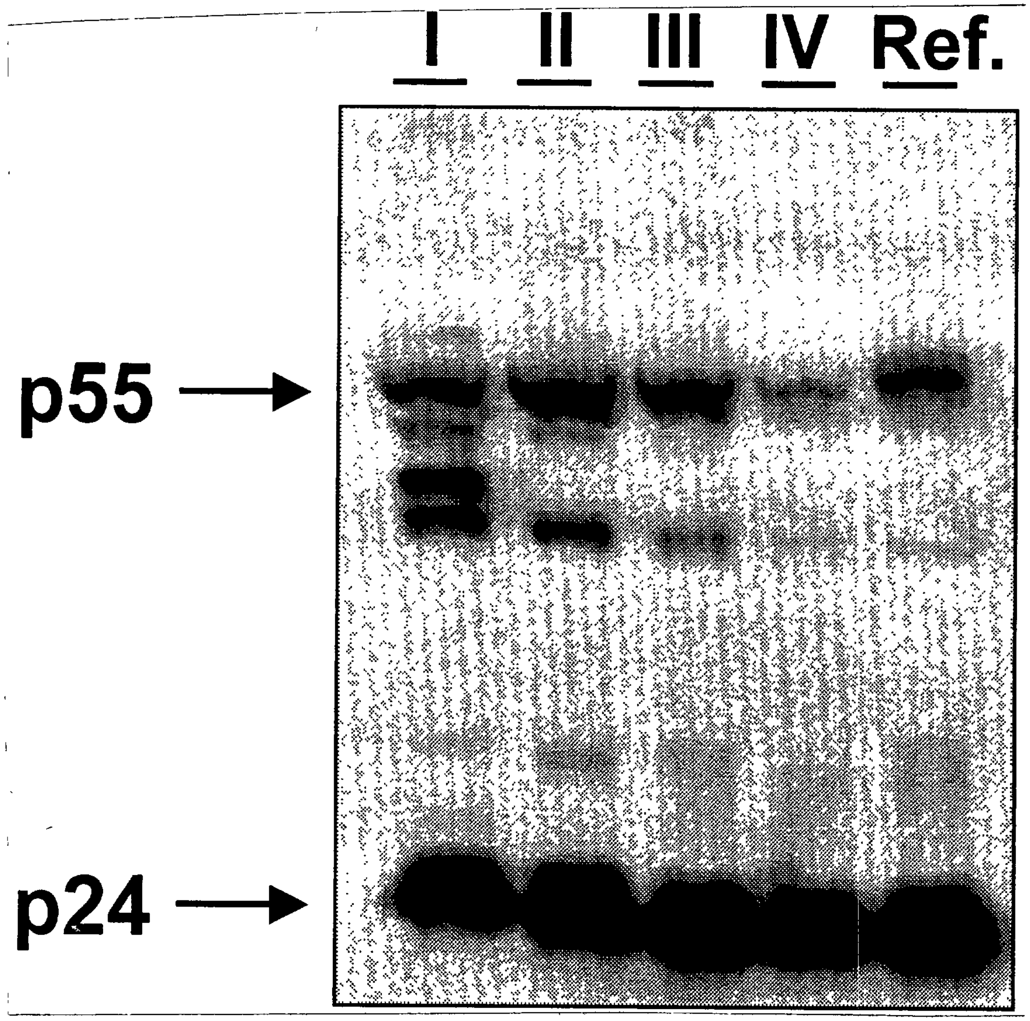
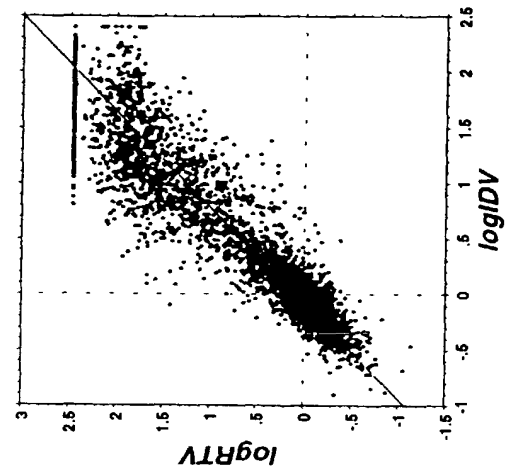


FIGURE 21

- HS to PIs is associated with decreased viral fitness
- In 25% of the cases analyzed in this study, the HS to PIs and decreased replication capacity was attributed to mutations in gag sequences flanking the N-terminus of PR
- Genotypic analysis revealed several unusual polymorphisms in p1-p6/TFP-p6* sequences
- Recombinant viruses carrying only the C-terminal gag sequences from patient isolates that retained the HS phenotype are released efficiently from the cell. However, analysis of the virus associated RT and PR activities suggest maturation defects

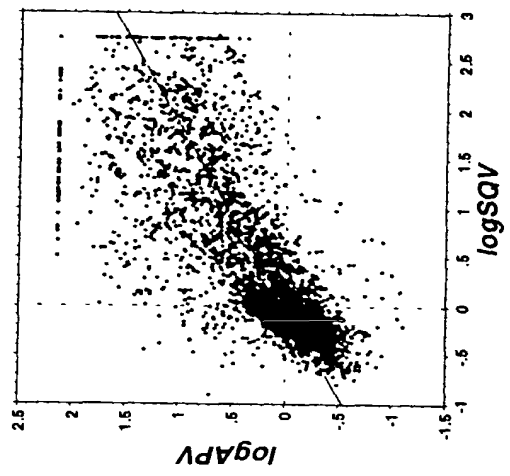
Applicants : Neil T. Parkin and Rainer Zhermann
U. S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 44 of 50

FIGURE 22



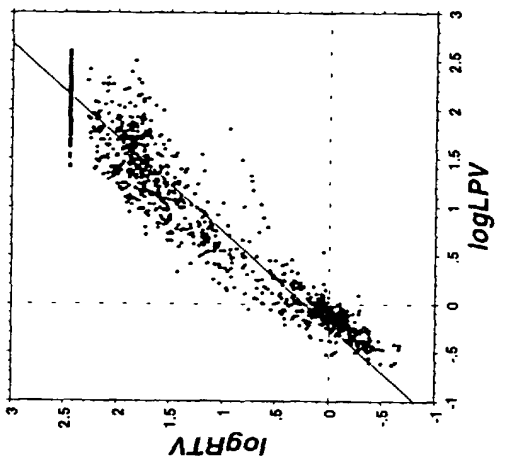
IDV vs. RTV

R^2=0.867



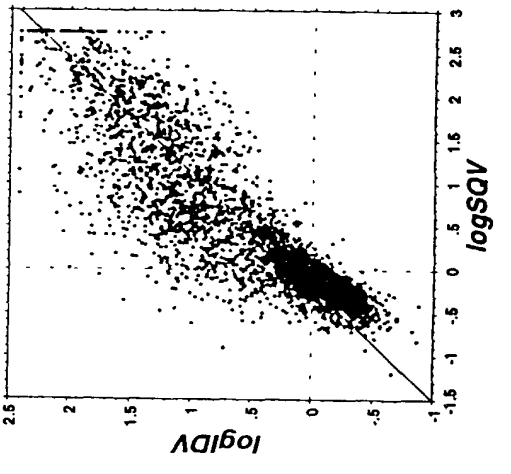
APV vs. SQV

R^2=0.591



LPV vs. RTV

R^2=0.921



IDV vs. SQV

R^2=0.784

Applicants : Neil T. Parkin and Rainer Ziermann
U.S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 46 of 50

FIGURE 23

R^2 values (sorted by drug)

PI 1	PI 2	R^2	
APV	IDV	0.675	
APV	LPV	0.777	
APV	NFV	0.544	
APV	RTV	0.737	
APV	SQV	0.591	
IDV	LPV	0.849	
IDV	NFV	0.774	
IDV	NFV	**0.925**	*
IDV	RTV	0.867	
IDV	SQV	0.784	
NFV	LPV	0.757	
NFV	RTV	0.696	
NFV	RTV	0.873	*
NFV	SQV	0 691	
NFV	SQV	0.801	*
RTV	LPV	**0.921**	
RTV	SQV	0.740	
RTV	SQV	0.880	**
SQV	LPV	0 678	

R^2 values (sorted by drug)

PI 1	PI 2	R^2	
IDV	NFV	**0.925**	*
RTV	LPV	**0.921**	
RTV	SQV	0.880	**
NFV	RTV	0.873	*
IDV	RTV	0.867	
IDV	LPV	0.849	
NFV	SQV	0.801	*
IDV	SQV	0.784	
APV	LPV	0 777	
IDV	NFV	0.774	
NFV	LPV	0.757	
RTV	SQV	0 740	
APV	RTV	0 737	
NFV	RTV	0 696	
NFV	SQV	0 691	
SQV	LPV	0 678	
APV	IDV	0 675	
APV	SQV	0 591	
APV	NFV	0 544	

R^2 values for pairwise comparisons (all samples)

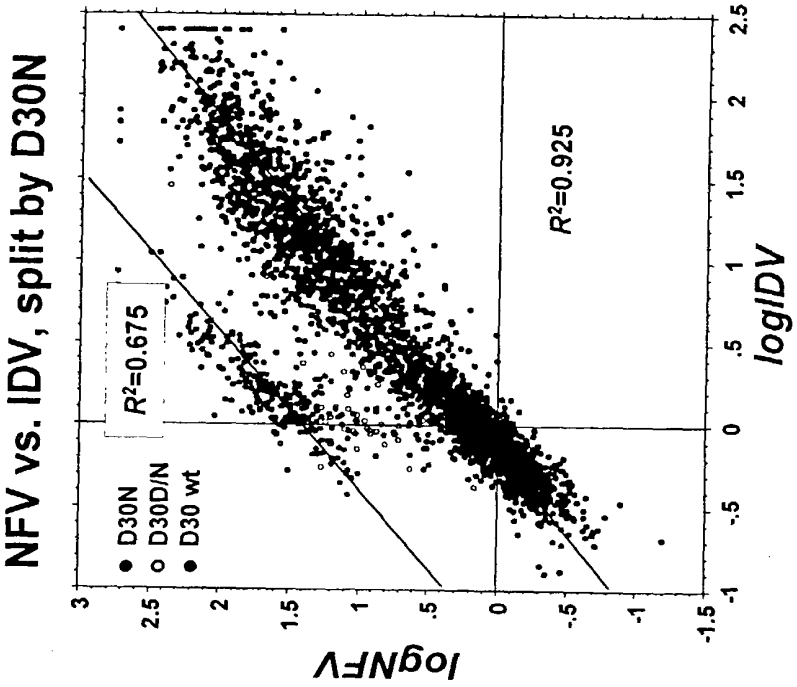
	APV	IDV	LPV	NFV	RTV	SQV
APV	1	0.675	0.777	0 544	0.737	0.591
IDV	0.675	1	0.849	0.774	0.867	0.784
LPV	0.777	0.849	1	0.757	**0.921**	0 678
NFV	0 544	0.774	0.757	1	0.696	0.691
RTV	0 737	0.867	**0.921**	0 696	1	0 740
SQV	0 591	0.784	0.678	0 691	0.740	1

<0.7
0 7-0.8
0.8-0.9
>0.9

* *Excluding viruses with D30N (see Fig.4)*

** *Excluding viruses with V82AFST (see Fig.5)*

FIGURE 25



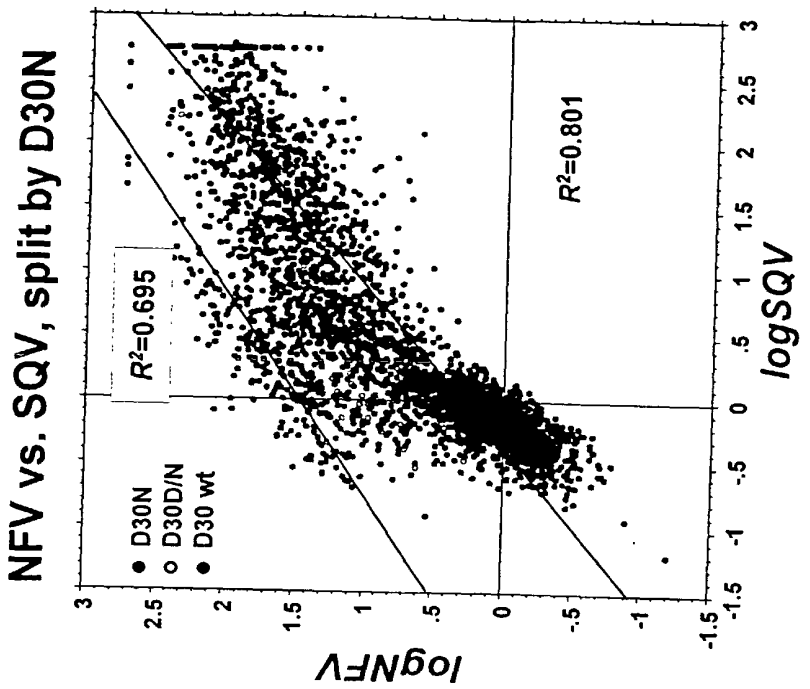
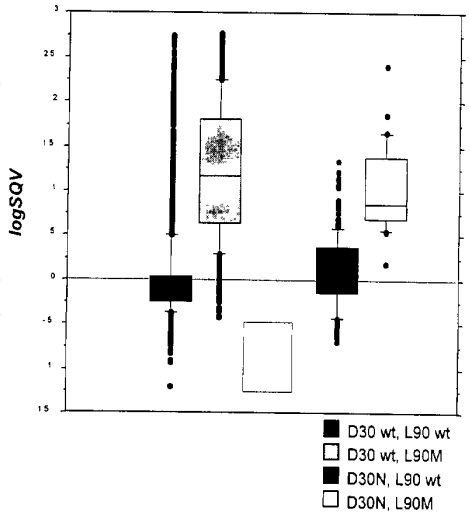


FIGURE 26

SQV fold change +/- D30N, L90M



Phenotypes of samples containing D30N, and/or L90M, from the database (boxes contain a bar at the median and represent the 25th to 75th percentiles; the error bars represent the 10th and 90th percentiles; and the dots are the outliers.

D30N/N88D/L90M: Patient samples

PR genotype (resistance-associated mutations)	Fold-change in IC_{50} vs. reference AMP	IDV	NFV	RTV	SQV
L10L/V, **D30N**, L33L/F, M36I, L63P, A71T, **N88D, L90M**	1.9	2.8	160.4	8.2	9.6
D30N, L63P, V77I, **N88D, L90M**	1.3	3.2	74.2	4.0	7.1
D30N, M36I, L63P, A71T, **N88D, L90M**	1.1	2.6	124.0	3.6	4.4
D30N, L63P, V77I, **N88D, L90M**	2.0	5.3	57.0	3.4	9.3
L10F, **D30N**, L33F, I54L, L63P, A71V, V77I, **N88D, L90M**	11.4	1.1	108.8	4.7	6.1
L10F/Y, D30N, I54L, L63P, A71T, V77I, N88D, L90M	3.7	3.9	171.4	5.7	38.1
D30N, L63P, V77I, **N88D, L90M**	0.4	1.3	32.8	2.1	3.7
L10F, D30N, L63P, A71T, V77I, N88D, L90M	2.3	7.6	217.5	3.9	11.9
L10L/R, D30N, M36I, I54V/L, L63P, A71V, N88D, L90M	2.7	5.2	140.1	10.2	21.0
D30N, M36I, I54V, L63P, A71V, **N88D, L90M**	1.5	5.8	218.5	16.8	24.3
K20K/R, **D30N**, M36I, F53F/L, I54V, L63P, A71V, **N88D, L90M**	2.3	8.4	>550	35.0	72.0
L10L/F, I13I/V, L19T, **D30N**, R41K, L63P, **N88D, L90M**	1.2	1.7	46.9	2.5	5.0
D30N, L63P, V77I, **N88D, L90M**	1.0	2.3	66.8	3.1	3.9
L10F, K20T, **D30N**, L33F, M36I, M46M/I, I54L, L63P, A71V V77I, **N88D, L90M**	27.6	6.8	>550	31.2	45.3
D30N, L33F, L63P, A71A/T, **N88D, L90M**	1.3	1.3	35.7	2.7	3.5
D30N, L63P, V77I, **N88D, L90M**	1.5	3.5	73.7	3.3	5.2
D30N, M36I, I54V, L63P, A71V, **N88D, L90M**	2.2	12.0	140.4	27.0	45.8
L10F, K20R, **D30N**, V32V/I, L33L/F/I, M36I, M46I, I47I/V, I54I/A/M/T/V, L63P, A71V, V82V/A, **N88D, L90M**	>130	>250	>550	>275	257.5

2.5-10 fold >10 fold

Phenotypes of samples containing D30N, N88D, and L90M. There are no mixtures detected at these sites, indicating that the mutations are linked. All have reduced susceptibility (>2.5-fold change in IC50) to NFV and SQV.

Applicants : Neil T. Parkin and Rainer Ziermann
U. S. Serial No. 09/874,472
Filing Date: June 4, 2001
Title of the Invention:MEANS AND METHODS FOR MONOTORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY AND GUIDING THERAPEUTIC DECISIONS IN THE TREATMENT OF HIV/AIDS
Sheet 47 of 50

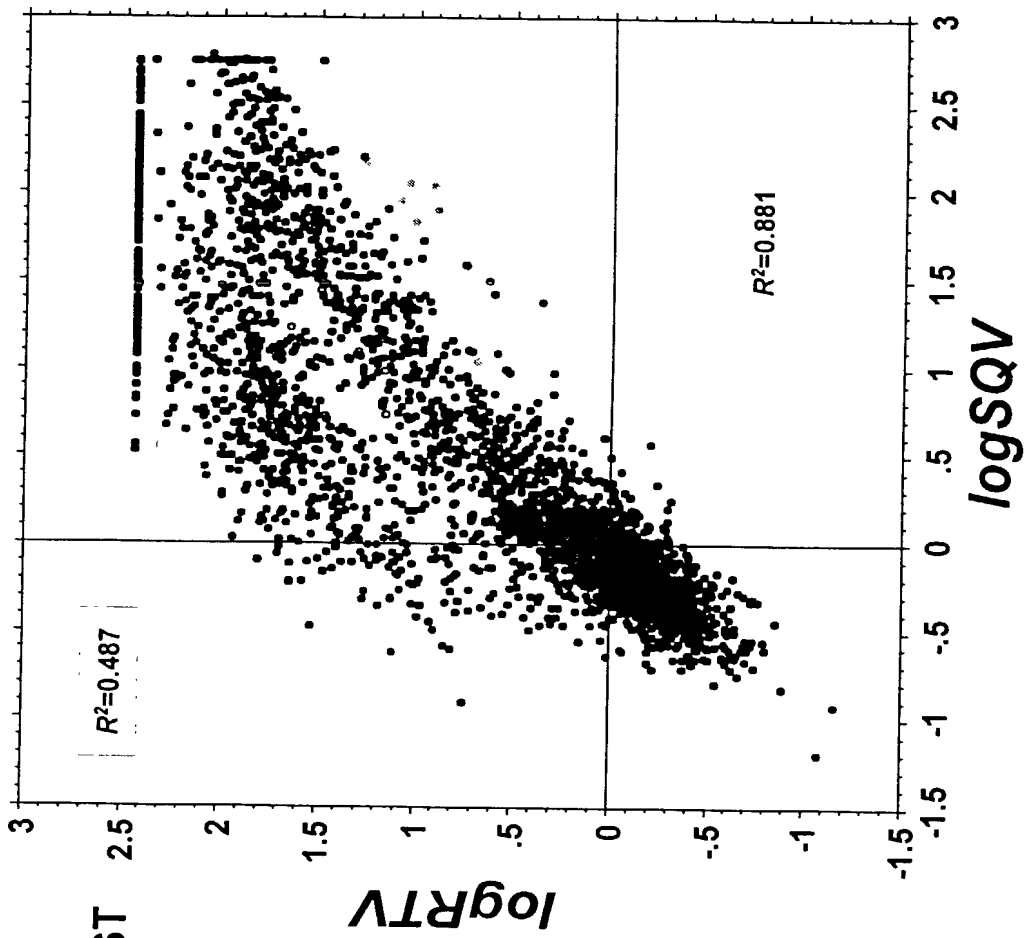


FIGURE 27

50/50

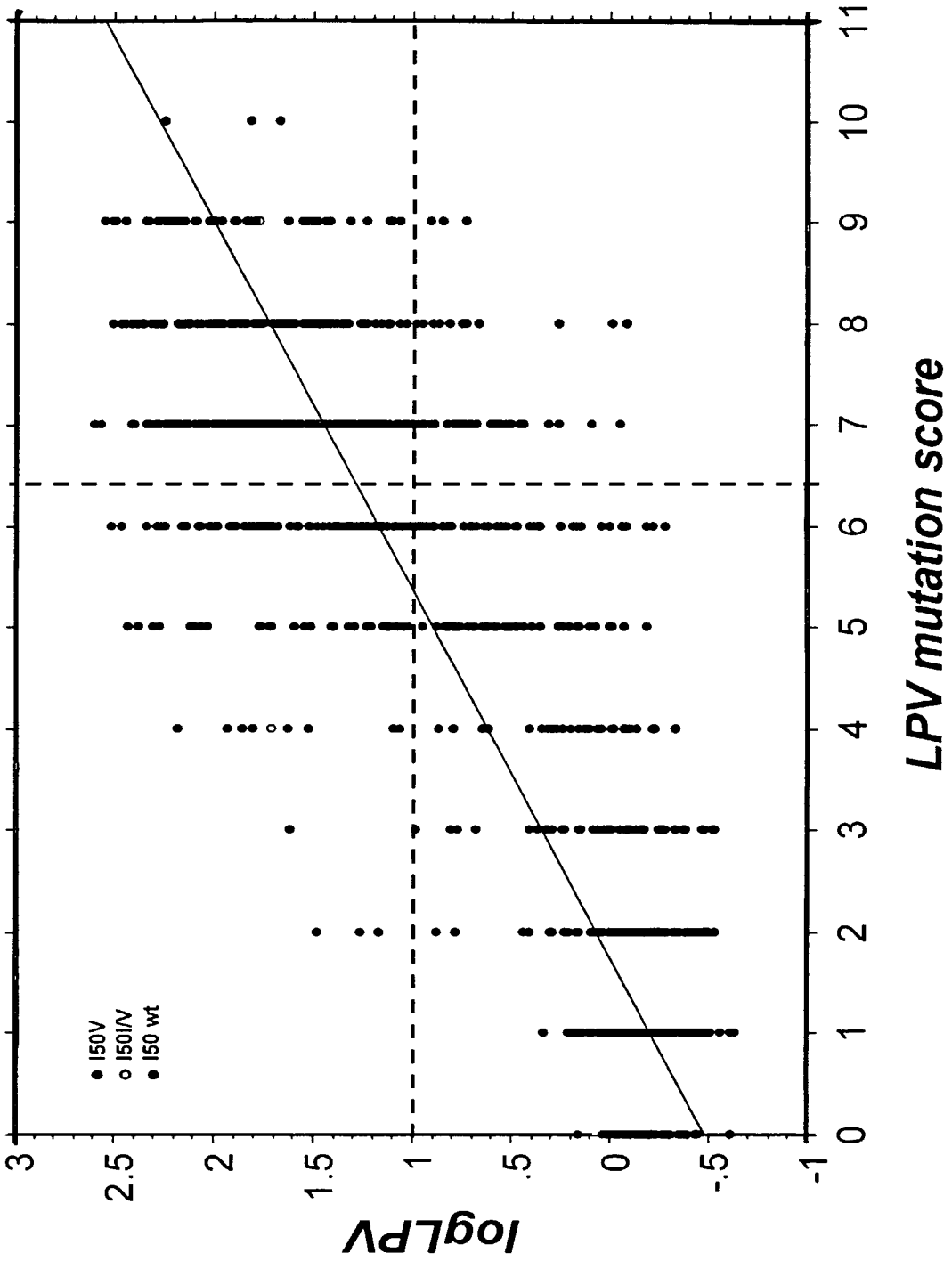


FIGURE 28